A Dissertation on

"INCIDENCE OF TRIPLE RECEPTOR STATUS (ER, PR, HER-2) IN PATIENTS UNDERGOING MASTECTOMY IN MMC&RGGGH, CHENNAI DURING 2012-2014 – A PROSPECTIVE AND RETROSPECTIVE STUDY"

BY

DR. P.SUBRAMANIAN

DISSERTATION SUBMITTED FOR THE DEGREE OF

MASTER OF SURGERY

BRANCH-1 (GENERAL SURGERY) AT

MADRAS MEDICAL COLLEGE, CHENNAI.

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY,

GUINDY,

CHENNAI – 600 032.

APRIL 2015.

CERTIFICATE

This is to certify that, the dissertation entitled "**INCIDENCE OF TRIPLE RECEPTOR STATUS (ER,PR,HER-2) IN PATIENTS UNDERGOING MASTECTOMY IN MMC&RGGGH, CHENNAI DURING 2012-2014 – A PROSPECTIVE AND RETROSPECTIVE STUDY**" is the bonafide work done by DR.P.SUBRAMANIAN during his M.S. General Surgery course 2012 – 2015, done under my supervision and is submitted in partial fulfillment of the requirement for the M.S. (BRANCH 1) – GENERAL SURGERY of the Tamilnadu Dr. M.G.R. Medical University, April 2015 examination.

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DECLARATION

I, **Dr. P.SUBRAMANIAN,** certainly declare that this dissertation titled "**INCIDENCE OF TRIPLE RECEPTOR STATUS (ER,PR,HER-2) IN PATIENTS UNDERGOING MASTECTOMY IN MMC&RGGGH, CHENNAI DURING 2012-2014 – A PROSPECTIVE AND RETROSPECTIVE STUDY**" represents a genuine work of mine. The contributions of any supervisors to the research are consistent with normal supervisory practice and are acknowledged. I also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, either in India or abroad. This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Master of Surgery degree Branch 1 (General Surgery).

Dr. P.SUBRAMANIAN

Date:

Place:

ACKNOWLEDGEMENT

I hereby wish to express my heartfelt gratitude to the following persons without whose help this study would not have been possible.

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I sincerely thank my family, my colleagues and junior post graduates for their help and support. Last but not the least I thank all my patients for their kind co-operation in carrying out this study successfully.

Dr. P.SUBRAMANIAN, M.S.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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CERTIFICATE OF APPROVAL

To
Dr. P.SUBRAMANIAN,
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Dear Dr. P.SUBRAMANIAN,

The Institutional Ethics Committee has considered your request and approved your study titled **"INCIDENCE OF TRIPLE RECEPTOR STATUS (ER, PR,HER-2) IN PATIENTS UNDERGOING MASTECTOMY IN MMC&RGGGH,CHENNAI DURING 2012-2014 – A PROSPECTIVE AND RETROSPECTIVE STUDY." No. 15082014.**

The following members of Ethics Committee were present in the meeting held on **05.08.2014** conducted at Madras Medical College, Chennai-3.

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11.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.
The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
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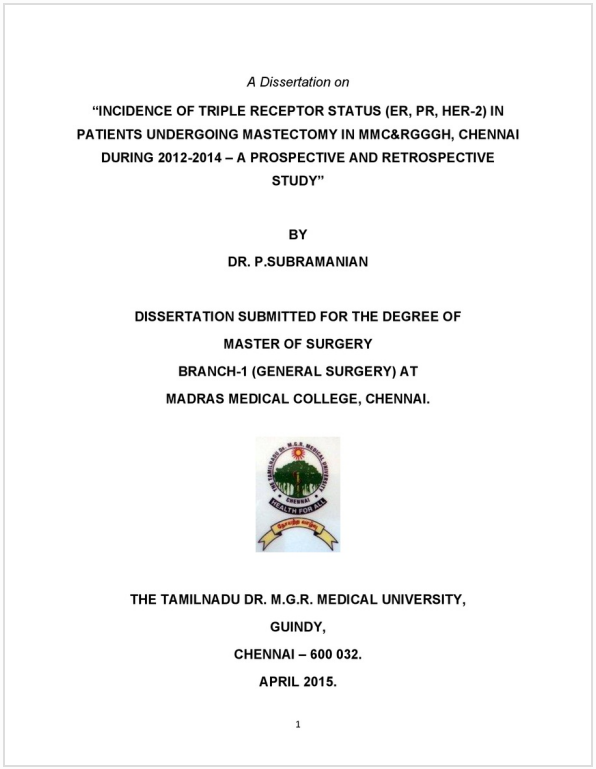

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APRIL 2015.

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CONTENTS

ABSTRACT

INTRODUCTION:

Hormone receptor status plays a very important role in deciding the need for appropriate hormonal therapy post surgically for patients with carcinoma breast and hence serves as an important prognostic factor. This study is done to determine the incidence of the three receptors namely Estrogen Receptor (ER), Progesterone Receptor (PR) and Her2/neu Receptor in women who underwent mastectomy for breast cancer in RGGGH, Chennai.

AIMS AND OBJECTIVES:

To study the incidence of receptor status in patients who underwent mastectomy for carcinoma breast in Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

PLACE OF STUDY:

Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

MATERIALS AND METHODS:

200 women who underwent mastectomy for carcinoma breast in my institution during 2012-2014 and had their specimen analysed for receptor status were included in the study. 120 belonged to premenopausal and 80 belonged to the postmenopausal age group. The parameter analysed was the presence or absence of the receptors either singly or in combination using special kits.

OBSERVATIONS AND CONCLUSIONS:

The incidence of Estrogen receptor positivity was found to be 57%. It was higher in premenopausal women (63.33%), whereas in postmenopausal women it was 47.5%.

The incidence of Progesterone receptor positivity was 32.5%. It was higher in postmenopausal women (36.25%) compared to premenopausal women (30%).

The incidence of Her2/neu receptor positivity was found to be 32.5%. It was equally distributed in premenopausal and postmenopausal women (32.5%).

The incidence of Triple negative receptor status was found to be 16%.

CONTENT

KEYWORDS

- Carcinoma breast
- Estrogen receptor
- Progesterone receptor
- Her2/neu receptor

INTRODUCTION

Breast cancer is the most common of all cancers and is the leading cause of cancer deaths in women worldwide, accounting for about 1.5% of all deaths. A recent study in India revealed that 1 in 28 women develop breast cancer during their lifetime. This is higher in urban areas accounting for 1 in 22 women compared to rural areas where it is much lower at 1 in 60 women. In India, the average age of the high risk group is 43-47 years, whereas in the west, those aged 53-57 yearsare more prone.

The overall incidence of breast cancer is on the rise as a result of increase in the life span, lifestyle changes and improved survival from other diseases. Despite this, the mortality is on the decline as a result of early detection by screening and improvements in therapy. Current treatment is guided by insights into breast cancer biology with an increase in the ability to define disease biology and status in individual patients and the availability of improved treatment modalities.

This is a prospective and retrospective observational study conducted at Rajiv Gandhi Government General Hospital, Chennai. The receptor status (namely ER, PR, HER 2 neu) of mastectomy specimen of those women operated for carcinoma breast were obtained and analyzed to determine the incidence of receptor status in the study population.

AIM OF THE STUDY

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To study the incidence of receptor status in patients who underwent mastectomy for carcinoma breast in Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

REVIEW OF LITERATURE

BRIEF SURGICAL HISTORY

- In 1600 B.C., Ebers Papyrus suggested heat cauterization of breast tumors.
- In 525 B.C., Democedes successfully treated a woman with breast cancer.
- In early 5^{th} and late 4^{th} century B.C., Hippocrates made detailed references to breast cancer and its effects.
- In 2^{nd} century A.D., Galen claimed that melancholia caused cancer. Treatment centered on nutrition and purgation. Surgical excision was only recommended if tumor was removable.
- In 1550s, Vesalius did wide excision and used ligatures for hemostasis.
- In 1560, Ambroise Pare recognized the relation between breast cancer and axillary node involvement.
- 1n 1786, Cruikshank described lymphatic drainage of breast.
- In 1845, Astley Cooper identified the suspensory ligaments of the breast which were named after him.
- In 1867, Moore proposed that local recurrence after breast amputation was due to disseminated fragments not removed at the

time of surgery. He suggested removal of breast along with the surrounding tissues.

- In 1870, Lister supported and refined Moore's technique of axillary exposure and divided pectoral muscles.
- In 1875, Volkmann proposed wide excision of breast along with the skin and pectoral fascia. In advanced cases, he removed pectoralis major and sometimes pectoralis minor muscle.
- In 1878, Billroth did lumpectomy for early breast cancer.
- In 1882, Halstead described radical mastectomy. He did axillary clearance in all cases and also removed the pectoralis major muscle in most of them giving wide margin of clearance.
- In 1885, Sappey noted the presence of sub areolar plexus into which parenchymal lymphatics drained, claiming that most of the drainage was to the axilla.
- In 1891, Welsh used frozen sections in the diagnosis of breast cancer.
- In 1895 , Czerny replaced a surgically removed breast with a large lipoma

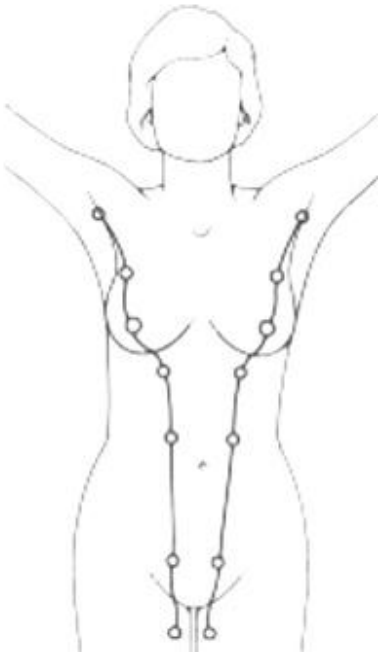
  (Breast reconstruction)

- In 1896, Tansini performed immediate breast reconstruction with Lattissmus Dorsi musculocutaneous flap after radical mastectomy.
- In 1897, Gocht irradiated a case of inoperable breast cancer.
- In 1899, Rotter noted metastasis while tracing lymphatics from breasts to interpectoral nodes.
- In 1918, Stibbe published detailed study on internal mammary lymphatics.
- In 1927, Handley suggested standard radical mastectomy be extended to include internal mammary lymphatics. He also implanted Radium tubes parasternally as prophylaxis.
- In 1938, Gershon-cohen recommended screening for breast cancer.
- In 1943, Patey and Dyson developed Modified Radical Mastectomy. They advocated wide skin incision and axillary clearance while sparing pectoralis major muscle.
- In 1948, McWhirter promoted the combination of simple mastectomy and high voltage x-ray therapy.
- In 1960, Egan described the modern mammography.
- In 1963, Dodd et al. performed the first needle – localization procedure.

- In 1965, Auchincloss and Madden described radical mastectomy preserving both pectoral muscles.
- In 1977, Dreaver pioneered breast reconstruction with myocutaneous flaps.
- In 1978, Bostwick described and popularized the use of Lattissmus Dorsi myocutaneous flap.
- In 1981, Turner and Maddox reported trials comparing radical vs modified radical mastectomy, finding no difference in survival.
- In 1981, breast conservation surgery was described.
- 1n 1992, Krag and Guiliano published the development of sentinel lymph node mapping in carcinoma breast.
- In 1994, BRCA1 wasdiscovered.
- In 1995, BRCA2 was discovered.
- In 2007, Bevacizumab was introduced as an adjuvant treatment in carcinoma breast.

EMBRYOLOGY

'MILK LINE' OF SCHULTZ



The breast is a group of large glands derived from the epidermis.

During the second month of gestation, two bands of thickened ectoderm appear on the ventral body wall extending from the axilla to the groin.

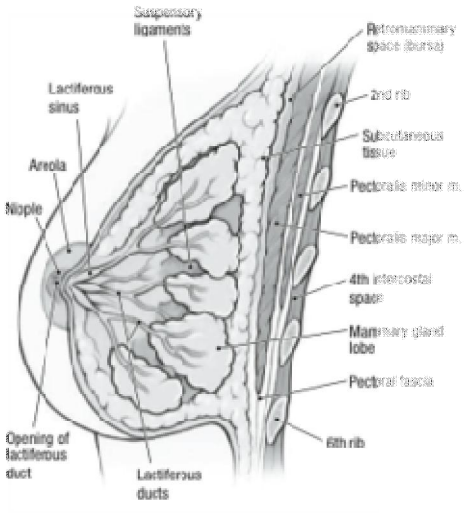
In humans, only the pectoral portion of the bands will persist and develop into adult mammary glands.

The glandular portion of the breast is derived from the ectoderm. It arises from local thickening of the epidermis from which 16 – 24 buds of

cells grow into the underlying mesoderm during the twelfth week. These ducts will become canalized near term to form lactiferous ducts.

The connective tissue stroma is derived from the mesoderm which also gives rise to dermis of the skin and the superficial fascia. Fibres forming the suspensory ligaments will develop from both the layers. This and the appearance of fat in the superficial fascia does not occur until puberty.

ANATOMY OF THE BREAST



- The female breast lies in the subcutaneous tissue (superficial fascia) of anterior thoracic wall.

- It extends from the sternal edge to near the mid-axillary line horizontally and from second to sixth ribs vertically.

- However, mammary tissue may extend from the clavicle to seventh or eighth ribs and from the midline to the anterior edge of lattissmus dorsi.

- It overlies the pectoralismajor, overlapping onto the serratus anterior and a small part of rectus sheath and external oblique muscle.

- A small extension of the upper outer quadrant towards the axilla is called the *Axillary Tail of Spence*. It may pass through a defect in the pectoral fascia called the *Foramen of Langer* which lies at the level of third intercostal space. It may be mistaken for an enlarged node or a lipoma.

- The breast is separated from the underlying muscle by a condensation of the superficial fascia called the *pectoral fascia***.**

- Strands of fibrous tissue connecting the dermis and the pectoral fascia running through the breast parenchyma are called the *suspensory ligaments*(**Cooper's ligaments**). They help to maintain the protuberance of the young breast.

- Behind the breast is the *Retro mammary space***(Chassaignac's bursa).** It is bound anteriorly by the deep layer of superficial fascia and posteriorly by the pectoral fascia. It contains loose areolar tissue and aids in the mobility of the breast on the chest wall.

- A *lobule* is the basic structural unit of the breast. They are more numerous in young women. They empty via ductules into the lactiferous ducts. These ducts are lined by contractile myoepithelial

cells and provided with a terminal dilation called the *ampulla / lactiferous sinus,* which serves as a reservoir for milk.

- About 15-20 *lactiferous ducts,* each draining a lobe, converge in a radial direction to open individually on the tip of the *nipple,* a projection just below the center of the breast, which contains smooth muscle fibres.

- The nipple is surrounded by circular pigmented skin called the *Areola,* which contains involuntary muscles.

- The areolar epithelium contains numerous sweat and sebaceous glands, the latter of which enlarge during pregnancy to form the *Montegomery's tubercles*.

- The male breast has no lobules or alveoli. The small nipple and areola overly the fourth intercostal space.

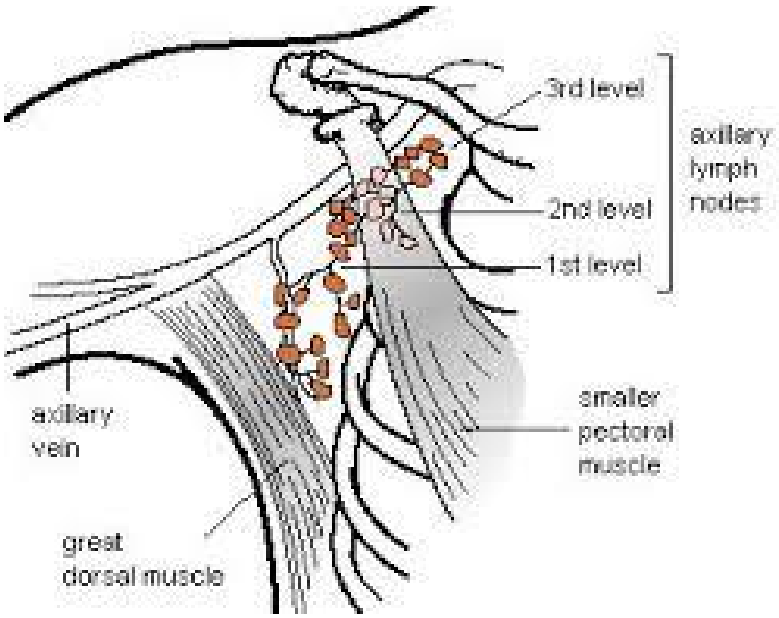
ANATOMY OF THE AXILLA

- It is a pyramidal space between the upper arm and the side of the thorax containing neurovascular structures and lymph nodes.
- It is bounded in front and behind by the axillary folds and communicates above with the posterior triangle of the neck.
- The **anterior wall** is formed by pectoralis major, pectoralis minor, subclavius muscles and the clavipectoral fascia.
- The **posterior wall** is formed by the teres major, latissimus dorsi and subscapularis muscles.
- The **medial wall** is formed by the upper four ribs and the intercostal muscles and the upper digitations of serratus anterior muscle.
- The **lateral wall** is formed by the intertubercular sulcus of the humerus related to the biceps brachii and coracobrachialis muscles.
- The **apex** is bounded by the superior border of scapula, outer border of first rib and posterior border of the clavicle; it forms the channel of communication between the neck and axilla.

- The **floor** is formed by the axillary fascia, which extends from the anterior to the posterior axillary folds and from the fascia over serratus anterior to deep fascia of the arm, and the skin.

- **<u>CONTENTS</u>:**

  - Axillary vessels,
  - Infraclavicular part of brachial plexus,
  - Long thoracic nerve,
  - Intercostobrachial nerve ,
  - Axillary lymph nodes and
  - Axillary pad of fat.



AXILLARY LYMPH NODES

- They are around 50 in number.
- They are divided into 3 levels
  - *Level 1* → lateral to pectoralis minor
  - *Level 2* → behind pectoralis minor
  - *Level 3* → medial to pectoralis minor

1. **Anterior or pectoral group**
   - Lie behind anterior pectoral fold , along lateral thoracic vessels
2. **Posterior or subscapular group**
   - Lie in relation to the posterior fold, along subscapular vessels.
3. **Lateral group**
   - Along medial side of Axillary vein

4. **Central group**

   - Situated in the fat of axilla

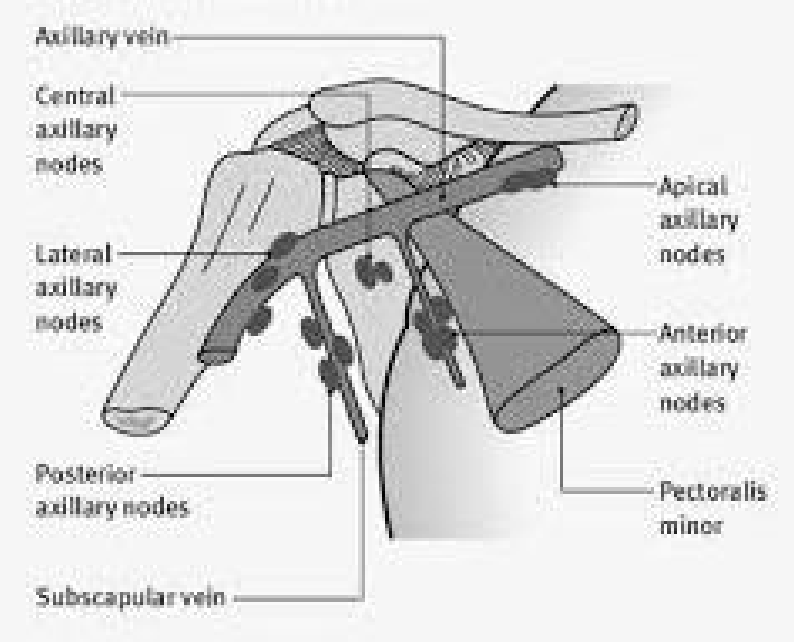
5. **Interpectoral (** ***Rotter's node)***

   - Between pectoralis major and minor.

6. **Apical group**

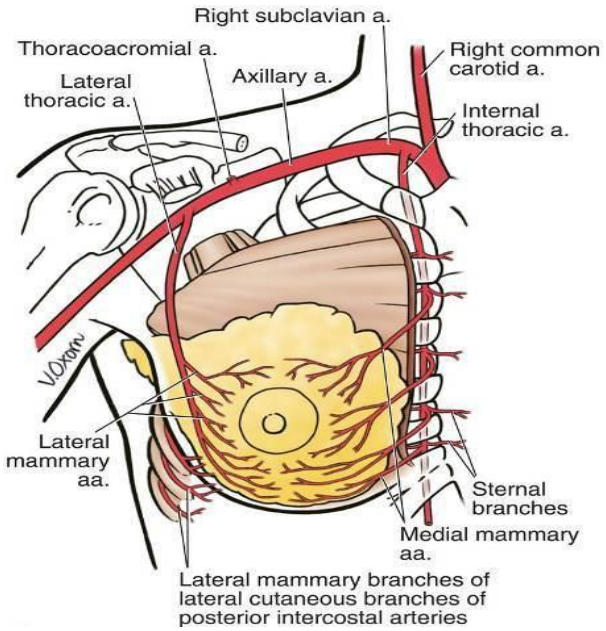
   - At the axillary apex.

AXILLARY NODES



BLOOD SUPPLY OF BREAST:

- Branches from lateral thoracic artery
- Perforating branches of internal thoracic artery
- Lateral branches of posterior intercostal arteries
- Occasionally, a branch from the Pectoral branch of thoraco-acromian artery.



VENOUS DRAINAGE OF BREAST:

- Occurs mainly to the axillary and internal thoracic veins via veins from glandular tissue and circumareolar venous plexus.

- Some drainage occurs to the posterior intercostal veins, which provides a link to the internal vertebral venous plexus serving a pathway for metastatic spread to the bone.

LYMPHATIC DRAINAGE OF THE BREAST

- A sub areolar plexus (**Sappey's plexus***)* of lymphatics communicates with lymphatics within the breast parenchyma.

- About75 % of the drainage passes to the axillary nodes mainly the anterior group.

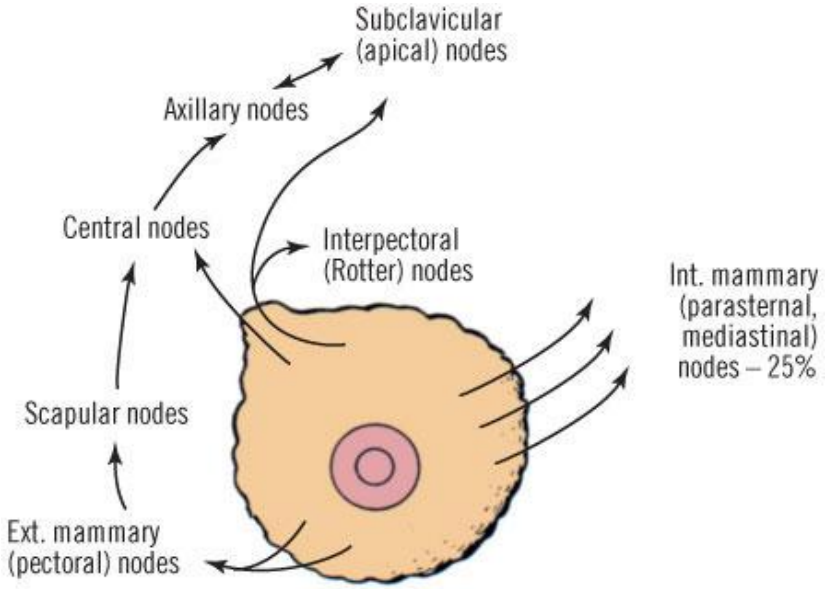
- Much of the rest, originating particularly from the medial part, drain into the internal mammary nodes.

- A few drain into the posterior intercostal nodes.

- Occasionally, some may drain into the interpectoral, infraclavicular and supraclavicular nodes.

- The superficial lymphatics have connections with that of the opposite breast and the anterior abdominal wall via which lymph may drain into posterior mediastinal nodes.

- The minor pathways convey lymph only when the major lymph channels are blocked by malignant disease.



NORMAL DEVELOPMENT AND PHYSIOLOGY

The breast development (*Thelarche*) begins between the ages of 9 and 12 years.

It is initiated by low amplitude pulses of pituitary gonadotropins which in turn increase the serum estrogen levels.

It is characterized by increased fat deposition, new duct formation and appearance of lobular units which is under the control of pituitary hormones, estrogen, progesterone, adrenal hormones, insulin & thyroxine.

The mature post pubertal breast comprises of stroma, lobular units, lactiferous ducts and fat.

During phases of menstrual cycle, the stroma and duct epithelium undergo cyclic stimulation resulting in alteration of morphology and hypertrophy. There is fluid accumulation and intralobularedema in late luteal phase which accounts for the breast engorgement and pain.

Pregnancy and lactation result in ultimate breast development under the influence of progesterone, prolactin and placental lactogen, which stimulate the development of secretory alveoli.

During lactation, prolactin causes secretion of milk proteins and lipids. Milk ejection occurs in response to neural stimulation initiated by sucking activity which causes release of oxytocin resulting in contraction of myoepithelial cells

When nursing ceases, prolactin levels fall and the non-ejected milk effects the cessation of milk production. The alveoli regress and the duct system returns to the non-pregnant state.

ANOMALIES OF THE BREAST

- **AMAZIA**

Absence of breast. May be associated with Turner's syndrome, congenital adrenal hyperplasia. *POLAND SYNDROME*→ constellation of amastia, absent sternocostal head of pectoralis major, syndactyly, nephropathy.

- **ATHELIA**

Absence of nipple.

- **POLYMASTIA or POLYTHELIA**

supernumerary breasts or nipples may develop along the 'milk line', most commonly in the inframammary fold region. It is due to incomplete involution of mammary ridge.

- **AMASTIA**

Complete absence of breast tissue, nipple and areola.

- **ABERRATIONS OF NORMAL DEVELOPMENT AND INVOLUTION (ANDI)**:

It occurs due to disturbance in cyclic hyperplasia or involution changes that occur in the breast, often bilateral.

It is seen in the 3rd and 4th decades of life.

It is common in spinster, nullipara and those who have not breast fed.

Its pathogenesis is not clear and wide range of processes occur such as fibrosis, adenosis, epitheliosis, cystic changes and inflammation in varying proportions on combinations.

The process begins with periductal fibrosis, probably secondary to estrogen stimulation, which causes irritation of cells lining the ducts and epithelial proliferation. Progressive epithelial clumping gives a gland-like appearance (adenosis) and obstruction to duct drainage causes cystic changes.

Its premalignant potential is debatable and the higher incidence of malignancy may be related to continued estrogen stimulation, which is common to both the conditions.

The various changes seen in different age groups are given below.

EARLY REPRODUCTIVE YEARS (15 – 25 YEARS)

NORMAL

- Lobular development
- Stromal development
- Nipple eversion

DISORDER

- Fibro adenoma
- Adolescent hypertrophy
- Nipple inversion

DISEASE

- Giant fibro adenoma
- Gigantomastia
- Sub areolar abscess

LATER REPRODUCTIVE YEARS (25 - 40 YEARS)

NORMAL

- Cyclical menstrual changes
- Nodularity
- Epithelial hyperplasia of pregnancy

DISORDER

- Cyclical mastalgia
- Bloody nipple discharge

DISEASE

- Incapacitating mastalgia

INVOLUTION (35 – 50 YEARS)

NORMAL

- Involution of lobules
- Involution of ducts
- Epithelial turnover

DISORDER

- Duct ectasia
- Nipple retraction
- Epithelial hyperplasia

DISEASE

- Periductal mastitis
- Epithelial hyperplasia with atypia

RELATIVE RISK FOR BREAST CANCER DEVELOPMENT IN ANDI

- **NON PROLIFERATIVE – NO INCREASED RISK**
    - Microcysts/ macrocysts
    - Duct ectasia
    - Simple fibroadenoma
    - Mastitis, Fibrosis
    - Apocrine metaplasia, Squamous metaplasia
    - Mild hyperplasia
- **PROLIFERATIVE – RR 1.5 TO 2.0**
    - Complex fibroadenoma
    - Ductal papilloma
    - Sclerosing adenosis
    - Hyperplasia – moderate/severe
- **PROLIFERATIVE DISEASE WITH ATYPIA – RR >2**
    - Atypical ductal hyperplasia
    - Atypical lobular hyperplasia

BREAST CANCER

CLASSIFICATION

NON-INVASIVE EPITHELIALCARCINOMAS:

- Lobular carcinoma in situ
- Ductal carcinoma in situ
  - Papillary type
  - Solid type
  - Cribriform type
  - Comedo type

INVASIVE EPITHELIAL CARCINOMAS:

DUCTAL

- Invasive Ductal carcinoma, NOS (not otherwise specified)
- Medullary carcinoma
- Mucinous or colloid carcinoma

- Tubular carcinoma
- Papillary carcinoma
- Scirrhous carcinoma
- Comedo carcinoma
- Inflammatory carcinoma
- Adenoid cystic carcinoma
- Metaplastic carcinoma

LOBULAR

- Invasive with predominant in situ component
- Invasive Lobular carcinoma

NIPPLE

- Paget's disease, NOS
- Paget's disease with intraductal carcinoma
- Paget's disease with invasive ductal carcinoma

MIXED CONNECTIVE AND EPITHELIAL CANCERS

- Cystosarcoma phylloides
- Angiosarcoma
- Carcinosarcoma
- Adenocarcinoma

RISK FACTORS FOR CARCINOMA BREAST

LOW RISK

- ✓ Early menarche
- ✓ Late menopause
- ✓ Nulliparity
- ✓ Hormone replacement therapy
- ✓ Alcohol use
- ✓ Smoking
- ✓ Post- menopausal obesity

INTERMEDIATE RISK

- ✓ First degree relative with breast cancer
- ✓ Late age at first child birth
- ✓ CHEK 2 mutation
- ✓ Proliferative breast disease

HIGH RISK

- ✓ BRCA 1 or BRCA 2 mutation
- ✓ LCIS
- ✓ Atypical ductal / lobular hyperplasia
- ✓ Radiation exposure before 40 years

DUCTAL CARCINOMA IN SITU (DCIS)

It is the most common type of non-invasive breast cancer consisting of malignant ductal epithelial cells which have not extended beyond the basement membrane.

It accounts for up to 25% of newly diagnosed breast cancers.

It comprises of a heterogeneous group of histopathological lesions classified based on architectural patterns, namely: micro papillary, papillary, solid, cribriform and comedo.

Very few cases present as a palpable mass and most commonly presents with discharge from the nipple.

Papillary and cribriform types are low grade lesions, whereas solid and comedo types are high grade lesions and associated with higher risk of invasive cancer.

Majority are diagnosed by mammography. The most common mammographic findings are calcifications (90%), which arise from intraductal debris formed by necrotic tumour cells and other debris. In 10% of cases, may present as soft tissue abnormalities as in invasive cancer.

The degree of atypia and presence of necrosis mainly determine the grade of malignancy which is given by *Van Nuys Prognostic Index*. It also takes into account the tumour size, resection margin and patient's age.

LOBULAR CARCINOMA IN SITU (LCIS)

It accounts for up to 15% of in situ cancers.

It is characterized by neoplastic cells which are confined to the lobules of the breast preserving their architecture.

It is asymptomatic and not detected by a mammogram.

It comes to attention only after a biopsy performed for some other reason.

It is frequently bilateral (40%) and mostly multicentric (70%).

It serves as a marker for identifying women at increased risk for development of subsequent invasive cancer, which is mostly ductal rather than lobular. The risk extends more than 20 years and is greater for the ipsilateral breast.

It is one of the indications for bilateral prophylactic mastectomy due to the above risk of cancer development in either of the breasts.

INVASIVE BREAST CANCER

When the neoplastic cells invade through the basement membrane into the stroma, it constitutes invasive breast cancer.

It is characterized histologically by lack of overall architecture, haphazard infiltration of cells into the stroma, formation of sheets of cells without conforming to form and function.

It is broadly divided into 2 groups: Invasive ductal and lobular cancers.

The most common type is the *Invasive ductal carcinoma, not otherwise specified (NOS) type*, which accounts for 50 – 70% of all breast cancers. The malignant cells don't take on special features as seen in the following types.

Tubular carcinoma is composed of infiltrating cells arranged in small glands lined by a single row of flat epithelium.

Mucinous or colloid carcinoma is characterized by secretion of copious amount of mucin by the tumor cells.

The above two types are low grade lesions and constitute about 2-3% of all breast cancers each.

Medullary carcinoma is characterized by malignant cells arranged in a syncytial fashion surrounded by an infiltrate of lymphocytes. It is a high grade type constituting about 5% of all breast cancers.

Invasive lobular carcinoma accounts for 10% of all breast cancers and is characteristically often bilateral and multicentric. It is the second most common histological subtype of breast cancer. It is of intermediate grade.

Inflammatory breast carcinoma is the most aggressive of all subtypes comprising about 5% of breast cancers. It is characterized by infiltration of the dermal lymphatic channels by infiltrating tumour cells. It is usually not associated with a breast lump making the diagnosis difficult. It manifests as edema, erythema, brawny induration and warmth mimicking breast abscess and hence at risk of being misdiagnosed.

Paget's disease accounts for about 1% of all breast cancers. It is characterized by malignant cells invading into the lactiferous sinuses onto the epidermis of the nipple. It presents with nipple erythema and irritation which progresses to ulceration and crusting. It is associated with an underlying breast cancer in >90% of cases. It is characterized by the presence of Paget's cells which are large pale staining cells with round or oval nucleus and a large nucleolus. It is managed by mastectomy or wide excision followed by radiotherapy.

FAMILIAL BREAST CANCER

Genetic factors account for about 5-10% of all breast cancer cases.

The most important genes are BRCA1 and BRCA2.

BRCA1 is a tumour suppressor gene located in chromosome 17. Mutations in this gene is responsible for up to 40% of familial breast cancers and is associated with up to 50% lifetime risk of ovarian cancer as well. These tumours tend to have a poor prognosis.

BRCA2 gene is located on chromosome 13 and its mutation accounts for 30% of familial breast cancers and 25% life time risk for ovarian cancer. It is also related to male breast cancer. These tumours tend to have a better prognosis compared to those with BRCA1 mutations.

Other predisposing genes include p53, PTEN, ATM, CHEK2, BRIP1, NBS1, RAD50, MSH2 and MLH.

SPREAD OF BREAST CANCER

LOCAL SPREAD

- to skin
- to pectoralis major muscle
- to chest wall

This can be identified by testing the fixity of the lump to the above structures by looking for cutaneous manifestations, restricted mobility on putting muscle into contraction or even at resting state and inability of the breast to fall forward on bending down.

HEMATOGENOUS SPREAD

- Bones → vertebrae (lumbar and dorsal), ribs, skull, ends of long bones; forming osteolytic metastasis.
- Liver
- Lungs
- Brain
- Adrenals**,** Ovaries

LYMPHATIC SPREAD

- Occurs primarily to the axillary nodes, particularly the anterior group.
- Tumours in the posteromedial aspect drain into the internal mammary nodes.
- Through dermal lymphatics, spread to contralateral nodes can occur.
- Involvement of supraclavicular and contralateral axillary nodes indicates advanced disease.
- Involvement of contralateral axillary nodes indicates metastatic breast cancer.
- Lymph node involvement serves as a marker for the metastatic potential and is the most important prognostic factor determining the outcome.

CLINICAL PRESENTATION

- Lump in the breast most commonly in the upper outer quadrant (50%)
- Recent Retraction of the nipple.
- Discharge from the nipple
    - Watery / bloody.
- Skin manifestations.
- Features of distant metastasis
    - Back pain/ bone pain/spontaneous fractures/ paraplegia
    - Dyspnea / cough with hemoptysis
    - Jaundice
    - Seizures
    - Headache
    - Krukenberg tumour
- Loss of appetite
- Loss of weight.

CUTANEOUS MANIFESTATIONS

- ✓ **Puckering / Dimpling of skin**
  - Due to infiltration of cooper's ligaments.
- ✓ **Retraction of nipple**
  - Due to infiltration of lactiferous ducts.
- ✓ **Peau d'orange appearance**
  - Due to obstruction of dermal lymphatics by tumour cells, the openings of hair follicles get buried in the oedema giving an orange peel like appearance.
- ✓ **Skin ulceration / fungation / Satellite nodules**
- ✓ **Nipple ulceration / scaling**
- ✓ **Cancer-en-cuirasse**
  - Multiple cancerous nodules & thickened skin like a coat of armour over chest & arms.

INVESTIGATIONS

'TRIPLE ASSESSMENT'

1. ***Clinical examination***

2. ***Radiological imaging***

   USG (young female)

   Mammography (older age)

   MRI

3. ***Pathological examination***

   FNAC

   Trucut / Core needle biopsy

   Surgical biopsy

❖ MAMMOGRAPHY

- It is a plain x-ray of breast soft tissue taken using low voltage(40 kV) and high ampere(300 mA) x rays
- Breast is compressed between two plexi glass plates to:
  - *Even out the thickness*
  - *Spread out tissue to decrease obscuration.*
  - *Lower x ray dose*
  - *Hold the breast still*
  - *Decrease x ray scatter*
- 2 views are taken :
  - Medio lateral oblique
  - Craniocaudal
- Dose of radiation is 0.1cGY and is quite safe.
- It is suited for older women as the breast is less dense (Fat absorbs little radiation & provides contrasting background for detection of small lesions.)
- Used for screening as well as diagnostic purposes

- It can be used for taking guided biopsy as in stereotactic core needle biopsy.

- ***Findings suggestive of malignancy:***
    - Mass effect
    - Architectural distortion
    - Loss of symmetry
    - Micro-calcification
    - Branching calcification
    - Clustering
    - Spiculation

BIRADS GRADING: (***B**reast **I**maging **R**eporting **A**nd**D**ata **S**ystem)*

- Grade I : Normal
- Grade II : Benign
- Grade III : Probably Benign
- Grade IV : Suspicious of Malignancy
- Grade V : Highly suggestive Malignancy
- Grade VI : Biopsy Proven Malignancy

DISADVANTAGE:

- Sensitivity is low in younger women as the breast is dense.
- Fails to detect15% of all palpable cancerous lumps.
- Thus a normal mammogram doesn't exclude the presence of carcinoma.

NEWER ADVANCES

- Digital mammography
- Computer aided detection
- Contrast enhanced mammography
- Tomosynthesis/ 3D mammography
- Xeromammography
- Optical mammography

These techniques help to delineate the lesions better and provide improved contrast enhancement.

❖ ULTRASOUND BREAST

- It is suited for young women with dense breasts.
- Its main use is to distinguish cystic from solid lesions.
- It has the highest sensitivity for axillary node detection.
- USG guided percutaneous biopsy of axillary nodes/lesions can be performed

DISADVANTAGE:

- It is highly operator dependent
- It is not used in screening as it fails to detect calcifications and misses a large number of cancers.

❖ MRI BREAST

It is used to

- Identify primary tumour in pts presenting with axillary lymphadenopathy without mammographic evidence of a primary tumour.
- For evaluating invasive lobular cancers.
- Useful to distinguish scar from recurrence in women who have had BCS for carcinoma previously.
- Useful as a screening tool in high risk women
- Best imaging modality of choice in women with breast implants.
- Used in taking guided biopsies.

Sensitivity varies from 60 % for DCIS to >90 % for invasive breast cancers.

DISADVANTAGE:

Less useful than USG in the management of axilla in both primary breast cancer as well as in recurrent breast cancers.

❖ FNAC*(FINE NEEDLE ASPIRATION CYTOLOGY)*

In FNAC, Cytology is obtained using 21G/23G needle and 10ml syringe with multiple passes in the lump with negative pressure in syringe. Aspirate is then smeared on to slide, air dried, fixed.

ADVANTAGES:

- Simple procedure
- Results can be obtained faster

DISADVANTAGES:

- High false positive and false negative results
- Invasive carcinoma cannot be differentiated from in-situ carcinoma.
- Does not provide information regarding the hormone receptor status.

USES:

- In recurrent breast cancer,
- For axillary nodes,
- In cases of diagnostic uncertainty.

❖ TRUCUT BIOPSY

Advantages over FNAC:

- Definitivediagnosis can be obtained.
- Helps to distinguish between invasive carcinoma and in situ carcinoma
- Useful in assessing the receptor status for hormone therapy.

❖ EXCISION BIOPSY

It is done in place of Trucut biopsy or when Trucut biopsy is not possible.

It is done for lesions smaller than 4 cm in size.

It provides complete histo-pathological diagnosis needed for treatment decision making.

It may serve as a definite procedure in the form of lumpectomy for benign tumours.

❖ INCISION BIOPSY

It is an alternate to Trucut biopsy when it comes as inconclusive and there is strong suspicion of malignancy.

It is done for lesions larger than 4 cm in size.

A small bit of tissue in removed making an incision in the skin over the lump.

The incision must be carefully placed so that the scar must be included within the incision for definitive surgery.

❖ STEREOTACTIC BIOPSY

It is done under the guidance of mammography using a vacuum assisted core needle.

The patient lies prone on a specially designed table for this procedure.

❖ SENTINEL LYMPH NODE BIOPSY

Sentinel lymph node is the first lymph node to drain the tumour.

It can be localized by pre-operative or per operative injection of vital blue dye (lymphazurin) with Technetium 99 radioisotope labeled sulphur colloid near the tumour or into sub dermal plexus around the nipple.

The markers are visually detected as blue staining with hand held gamma- camera and is biopsied with a small incision made directly over it and sent for frozen section analysis.

If the sentinel node is negative for metastasis, then the chance of other nodes to get affected is found to be remote.

It has been found to have low false negativity rates and hence helps to avoid unnecessary axillary dissection if node is negative for metastatic deposits.

It forms a part of the staging workup in cases of clinically imperceptible nodes to look for micro / macro metastasis.

STAGING WORKUP

CHEST X RAY / CT CHEST

Pleural effusion, Cannon-ball secondaries, Mediastinal lymph nodes.

USG/CT ABDOMEN

Liver metastasis, Ascites, Krukenberg tumour

SKELETAL SURVEY / BONE SCAN

Osteolytic secondaries

LFT

Mammogram of opposite breast

FNAC of contralateral axillary nodes

CA 15-3 / CEA

Elevated in metastatic breastcancer

TNM STAGING

PRIMARY TUMOUR

Tx : Primary tumour cannot be assessed

T0 : No evidence of primary tumour

Tis : Carcinoma in situ (DCIS , LCIS , Paget's disease)

T1 : Tumour ≤ 20 mm in greatest dimension

T1mic : Tumour <1 mm in greatest dimension

T1a : Tumour >1 mm but ≤ 5 mm in greatest dimension

T1b : Tumour >5 mm but ≤ 10 mm in greatest dimension

T1c : Tumour >10 mm but ≤ 20 mm in greatest dimension

T2 : Tumour > 2 cm but ≤ 5 cm in greatest dimension

T3 : Tumour > 5 cm in greatest dimension

T4 : Tumour of any size with direct involvement of chest wall and/or

skin; inflammatory carcinoma

T4a : Extension to chest wall (ribs, intercostals, serratus anterior)

T4b : Extension to skin (ulceration/ satellite nodules/

peau d'orange)

T4c : T4a + T4b

T4d : Inflammatory carcinoma

REGIONAL LYMPH NODES (CLINICAL)

Nx : nodes cannot be assessed

N0 : no regional nodes

N1 : ipsilateral mobile axillary node

N2a : ipsilateral axillary nodes fixed to one another or other structures

N2b : clinically apparent internal mammary nodes in the absence of

clinically palpable axillary nodes

N3a : ipsilateral infraclavicular nodes with or without axillary nodes

N3b : ipsilateral internal mammary nodes and axillary nodes

N3c : ipsilateral supraclavicular nodes with or without axillary or internal mammary nodes

REGIONAL LYMPH NODES(PATHOLOGICAL)

pNX: Regional lymph nodes cannot be assessed.

pN0: No regional node metastasis detected histologically and no examination for Isolated tumour cells.

pN0(I-) : No regional node metastasis histologically ; negative IHC

pN0(I+) : Malignant cells in regional lymph nodes no greater than 0.2 mm (detected by H&E stain or IHC)

pN0(mol-) : No regional node metastasis histologically ; negative molecular findings(RT–PCR)

pN0(mol+) : Positive molecular findings but no regional node metastasis detected by histology or IHC

pN1: metastasis in one to three axillary nodes and/or internal mammary nodes with microscopic disease detected by SLNBbut not clinically apparent

pN1mi : Micrometastasis (>0.2 mm &/or >200 cells; none >2.0 mm)

pN1a : Mets in 1-3 axillary nodes at least one > 2.0 mm

pN1b : Mets in internal mammary nodes detected by SLNBbut not clinically

pN1c : pN1a + pN1b

pN2: metastasis in four to nine axillary nodes or in clinically apparent internal mammary nodes in the absence of axillary nodal metastasis.

pN2a : Mets in 4-9 axillary nodes at least one > 2.0 mm

pN2b : Mets in clinically detected internal mammary nodes in the absence ofaxillary nodes

pN3: metastasis in 10 or more axillary nodes or in infraclavicular nodes or in clinically apparent internal mammary nodes in the presence of axillary nodes or in more than three axillary nodes with clinically negative micrometastasis in internal mammary nodes or in ipsilateral supraclavicular nodes.

pN3a : Mets in ≥ 10 axillary nodes (at least one > 2 mm) or metastasis to infraclavicular nodes

pN3b: Mets in clinically detected internal mammary nodes in the presence of one or more positive axillary nodes; or in > 3 axillary nodes & in internal mammary nodes detected by SLNB.

pN3c: Metastasis in ipsilateral supraclavicular lymph node.

DISTANT METASTASIS

Mx: Metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

AJCC STAGE GROUPING

STAGE	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T0 T1	N1mi	M0
IIA	T0 T1	N1	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0 T1 T2	N2	M0
	T3	N1 N2	M0
IIIB	T4	N0 N1 N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

CLASSIFICATION BASED ON TNM STAGING

- **Early breast cancer**

Stages IA, IB, IIA, IIB (T2 N1 M0)

It includes tumours less than 5 cm in size with/without ipsilateral mobile axillary nodes in the absence of distant metastasis.

- **Locally advanced breast cancer**

Stages IIB (T3 N0 M0), IIIA, IIIB, IIIC

It includes tumours more than 5 cm in size; ipsilateral fixed axillary nodes or palpable internal mammary, infraclavicular or supraclavicular nodes; fixity to skin/chest wall; inflammatory carcinoma.

- **Metastatic breast cancer**

Stage IV

It includes tumours with distant metastasis irrespective of tumour size or nodal status.

MANCHESTERSTAGING

***STAGE 1*:**

Tumour confined to the breast; no muscle/chest wall/ nodal involvement. Skin involvement < tumour size.

***STAGE 2*:**

Tumour confined to the breast with the presence of palpable mobile axillary nodes. Skin involvement < tumour size.

***STAGE 3*:**

Tumour extends beyond the breast parenchyma.

- Skin infiltration over a large area compared to the size of the breast or skin ulceration.
- Fixation to underlying fascia or muscle.

Axillary nodes, if palpable, are mobile.

***STAGE 4*:**

Tumour extends beyond the breast in the form of skin infiltration beyond the breast, chest wall fixation, fixed axillary nodes, palpable supraclavicular nodes, spread to opposite breast/axilla and presence of distant metastasis.

PROGNOSTIC FACTORS

TUMOUR RELATED FACTORS

- Axillary nodal status
- Tumour size
- Histological grade
- Lympho-vascular invasion
- Hormone receptor status
- DNA content
- Growth factor indicators – erb B2, EGFR
- Factors related to growth rate – S-phase fraction, p53
- Factors related to invasion – cathepsin D, collagenase
- Factors related to cell adhesion – CD44 gp.

The *axillary nodal status* and *tumour size* are the two most important factors determining the prognosis.

HOST RELATED FACTORS

- Age
- Menopausal status
- Family history (first degree relatives)
- Personal history of breast cancer
- Nutrition
- Immunosuppression
- Prior chemo / radiotherapy

AXILLARY NODAL STATUS

It is the single most important prognostic factor.

The 10 year survival rate is 75% for node negative disease but drops to 50% if 1-3 nodes are involved and to less than 25% if ≥ 4 nodes are involved.

Involvement of contralateral axillary nodes indicates metastatic breast cancer and very poor prognosis.

TUMOUR SIZE

It is the second most important prognostic factor.

Larger the size of the tumour, higher the recurrence rate and lower the disease free survival rate and hence poorer the prognosis.

GRADE OF THE TUMOUR

Nottingham or Elston-Ellis modification of Scarff-Bloom-Richardson system is commonly used for grading.

It takes into account 3 factors: tubule formation, nuclear pleomorphism and mitotic rate.

Each is assigned a value of 1-3 points and the final score is obtained by adding up the score for each of the 3 factors.

GRADE 1 (3-5 points) → well differentiated

GRADE 2 (6/7 points) → moderately differentiated

GRADE 3 (8/9 points) → poorly differentiated

Higher grade tumours need to be treated more aggressively and have worse survival rates.

RECEPTOR STATUS

Hormone receptor status is critical in determining the suitability for targeted therapy in patients with breast cancer before or following surgery.

The presence of receptors, namely ER, PR and Her2-neu, is determined by immunohistochemistry (IHC) method.

The breast cancer can be classified into 4 main types based on the receptor status as:

- Luminal A,
- Luminal B,
- Her2/neu overexpression and
- Basal-like/Triple negative.

MOLECULAR SUBTYPES

MOLECULAR SUBTYPE	CLINICO PATHOLOGIC DEFINITION
LUMINAL – A	Luminal-A like • ER + • HER 2 –ve • PR high • Ki67 low
LUMINAL – B	Luminal-B like (HER 2 negative) • ER + • HER 2 –ve • PR low or Ki67 high
	Luminal-B like (HER 2 positive) • ER + • HER 2 +ve • Any PR or any Ki67
HER 2 OVEREXPRESSION	HER 2positive (non-luminal) • HER 2 positive • ER & PR absent
BASAL – LIKE	Triple negative • ER & PR absent ; HER 2 –ve

ER positive tumours depend on estrogen for their growth and thus can be treated with drugs which either block the action of estrogen or decrease its level in the blood. They tend to have a better prognosis.

Her2 positive tumours can be treated with targeted therapy against Her2/neu receptor and generally have a poorer prognosis.

Triple negative tumours have the worst prognosis.

TUMOUR TYPE

Invasive Mucinous and tubular cancers have a better prognosis compared to comedo or NOS type.

Invasive lobular cancer has intermediate prognosis.

Invasive medullary cancer has a poor prognosis.

TUMOUR STAGE

Higher the stage, worse the prognosis.

MANAGEMENT

The management of breast cancer is multimodal comprising of surgery, chemotherapy, radiotherapy, hormone therapy and targeted therapy.

SURGERY

The various surgical methods include

- Radical mastectomy
- Modified radical mastectomy
- Simple mastectomy
- Breast conservation surgery.

❖ *RADICAL MASTECTOMY*

It was first described by Halstead in 1894.

It comprises of removal of the breast tissue with nipple-areolar complex, level I, II and III axillary nodes, pectoralis major and minor, subscapularis, portions of serratus anterior, lattissmus dorsi, external oblique and rectus muscles.

The structures preserved include the axillary vessels and cephalic vein.

- Disadvantages:
    - ✓ Highly mutilating surgery
    - ✓ Shoulder fixation
    - ✓ Lymphedema of arms
    - ✓ Winging of scapula
    - ✓ Poor cosmetic results

It is seldom being done now-a-days.

❖ ***MODIFIED RADICAL MASTECTOMY***

It was first described by Patey in 1943.

It comprises of removal of the entire breast tissue, nipple-areolar complex, skin over the breast, pectoralis minor muscle, level I to III nodes.

- AUCHINCLOSS MODIFICATION:

Pectoralis minor muscle retracted (preserved) and only level I and II nodes are removed.

- SCANLON MODIFICATION:

Pectoralis minor muscle cut at its insertion to remove level III nodes as well and sutured back.

The structures preserved include the axillary vessels, long thoracic nerve of Bell, thoracodorsal nerve, cephalic vein and pectoralis major muscle.

It is less morbid and cosmetically better and provides good vascular bed for reconstruction compared to the radical mastectomy.

Adequate axillary clearance is when more than ten axillary nodes are present in the resected specimen and the presence of more than 4 positive nodes indicates poor prognosis.

It is the most common surgery being performed for carcinoma nowadays.

❖ ***SIMPLE MASTECTOMY***

It involves removal of whole breast with nipple areolar complex

Sentinel node surgery for axillary staging may be done through same or separate incision.

It is done prophylactically in carriers of familial breast cancer gene mutations (BRCA1 and BRCA2)

- TOILET MASTECTOMY

  Done in locally advanced fungating or ulcerated breast cancer for improving the morbidity.

❖ ***BREAST CONSERVATION SURGERY***

It was first introduced in 1981.

It is being used in the management of early breast cancer {stage 1 and 2}.

It comprises of removal of the lump with adequate margin of clearance, assessment of axillary nodal status and post-operative radiotherapy.

It may be in the form of wide local excision, quadrantectomy and partial mastectomy.

- WIDE LOCAL EXCISION:

  Removal of the tumour with a rim of 1 cm of normal breast tissue followed by radiotherapy.

- QUADRANTECTOMY:

  Removal of the quadrant of the breast containing the tumour.

- PARTIAL/SEGMENTAL MASTECTOMY:

  Removal of the tumour along with some amount of surrounding normal breast tissue and the fascia over the underlying muscle.

- QUART THERAPY OF VERONESI:

  It comprises of *Qu*adrantectomy, *A*xillary node dissection and *R*adio*t*herapy.

The indications for breast conservation surgery include smaller monocentric tumours, small size of the tumour relative to that of the breast, patients' compliance for adjuvant radiotherapy.

The contraindications include large tumour size, multicentric tumours, diffuse micro calcifications, pregnancy, familial breast cancer, previously irradiated chest wall, invasive lobular carcinoma, LCIS, collagen vascular diseases.

It is cosmetically superior to MRM and being considered as a standard treatment for early stage breast cancer.

BREAST RECONSTRUCTION

It is done following mastectomy to improve the cosmetic appearance of the chest.

It can be done using

- ***Breast implants***

  Made of silicone and placed subcutaneously or subpectorally.

- ***Tissue expanders***

- ***Flaps***

  - Lattissmus dorsi flap
  - TRAM flap (transverse rectus abdominis myocutaneous flap) → pedicle or free flap based on superior or inferior epigastric arteries respectively.

The advent of microsurgical techniques have made free flaps a standard mode of reconstruction.

CHEMOTHERAPY

It can be adjuvant (given after surgery) or Neoadjuvant (given before surgery).

Neoadjuvant therapy is useful in downsizing locally advanced cancers to improve the resectability and also helps to assess the response of the tumour to the chemotherapeutic agents. It is usually given for 3 cycles.

Adjuvant chemotherapy is indicated for

- All node positive cancers,
- Tumours larger than 1 cm in size,
- Hormone nonresponsive/ receptor negative tumours.

It is given for 6 cycles.

Palliative chemotherapy is indicated in widespread metastatic breast cancer.

The chemotherapeutic agents used are broadly divided into Anthracyclines and non- Anthracyclines.

The commonly used chemotherapeutic regimens include **FAC** (5-fluorouracil, Adriamycin and cyclophosphamide) and **CEF** (cyclophosphamide, epirubicin and 5-fluorouracil).

RADIOTHERAPY

Indications:

- Positive resection margins
- Following breast conservation surgery
- Chest wall involvement
- For internal mammary nodes
- When axillary clearance is not done
- For metastasis (bone , brain)

It is contraindicated to axilla following axillary dissection due to increased risk of lymphedema of arms.

Adverse effects:

- lymphedema of arms
- cancer-en-cuirase
- lymphangiosarcoma (Stewart Treves syndrome)

Dose: 5000-6000 cGy units (to chest wall)

200 cGy per day for 5 days a week for 5-6 weeks (to the axilla - when dissection has not been done)

HORMONE THERAPY

It is indicated in receptor positive breast cancers.

❖ *TAMOXIFEN*

- It is a Selective Estrogen Receptor Modulator.
- It has Anti-estrogen action in the breast & agonistic action elsewhere.
- It acts by blocking cytosolic estrogen receptors.
- Its Half-life is 7 days and takes 4 weeks to show its effects.
- It also reduces cholesterol levels & cardiovascular morbidity.
- It is used for adjuvant hormone therapy in premenopausal women with ER positive breast cancer.
- Its dosage is **10 mg BID or 20 mg OD orally for5 years.**

- Other drugs with similar mechanism of action are **Raloxifene, Ormeloxifene**.

- ***Adverse effects***

  - Tamoxifen flare(flushing,sweating,vaginal dryness, itching).

  - Bone pain and weight gain.

  - Increased incidence of endometrial cancer.

  - Increased risk for DVT (3%).

  - Increased incidence of pulmonary embolism, CVA, TIA, cataract, fractures.

LETROZOLE

- It is a non-steroidal competitive inhibitor of enzyme "aromatase" which converts adrenal androgens to estrogens – 'Aromatase Inhibitor.'

- Other drugs with similar action include **Anastrazole** and **Exemestane (**steroidal).

- It is used as adjuvant endocrine therapy in post-menopausal women with hormone responsive breast cancer.

- It is also useful in metastatic & recurrent cases.
- It slows down & stops the growth of estrogen sensitive breast tumours by reducing estrogen level by up to 98%.
- Half-life is 45 hours.
- It decreases the bone density.
- Its dosage is**2.5mg once daily orally for 5 years**.
- ***Side effects***

  Vaginal dryness, night sweats, hot flushes, vaginal bleeding, cardiovascular problems & osteoporosis.

The other modes of hormonal therapy include

- ✓ GnRH analogues (goserelin, buserelin)
- ✓ Ovarian ablation
- ✓ Oophorectomy
- ✓ Adrenalectomy

TARGETED THERAPY

❖ *TRASTUZUMAB (HERCEPTIN)*:

- It is a recombinant humanized monoclonal antibody that blocks HER-2/Neu receptors thereby preventing the growth of cancer cells.

- Used in combination with chemotherapy in Her2 positive breast cancers.

- It is given by IV infusion: **4mg/kg as loading dose**&**2mg/kg as maintenance dose weekly**along with Chemotherapy & then **6mg/kgonce in 3 weeks**for **1 year**.

- Its main side effect is Cardiomyopathy especially when combined with anthracycline based chemotherapy.

❖ *LAPATINIB*

It is an EGF receptor antagonist that can be used in Metastatic disease in combination with Trastuzumab.

❖ *BEVACIZUMAB*

It is a VEGF receptor antagonist recently being tried in breast cancer.

TREATMENT APPROACH

LCIS

Observation with or without Tamoxifen.

DCIS

Mastectomy → if widespread involvement

Wide excision + radiotherapy → for limited disease

EARLY BREAST CANCER

i. MRM + adjuvant chemotherapy + radiotherapy

OR

ii. Breast conservation surgery + assessment of axillary nodal status + radiotherapy

- Adjuvant Hormone therapy is given based on receptor status positivity.

LOCALLY ADVANCED BREAST CANCER

If operable

i. MRM + adjuvant chemotherapy + radiotherapy

OR

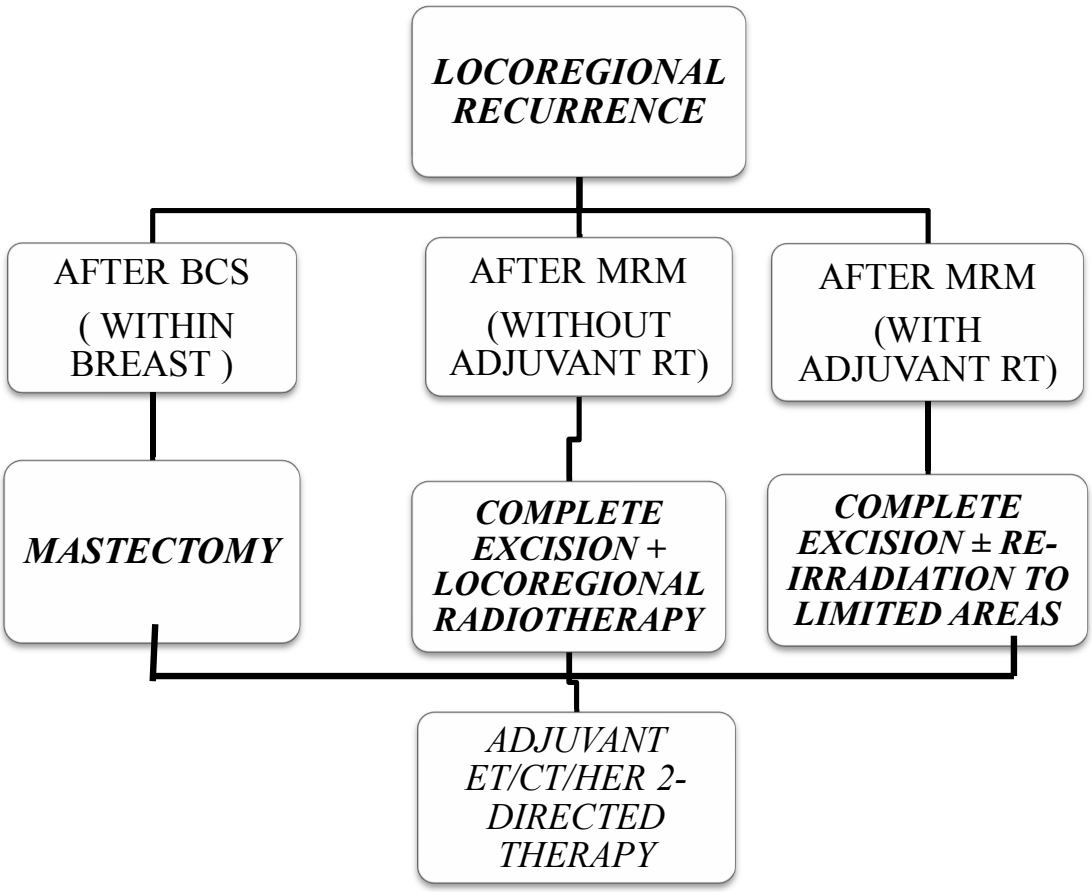
ii. Neoadjuvant chemotherapy + MRM + adjuvant chemotherapy + radiotherapy

If inoperable

Neoadjuvant chemotherapy + MRM if possible + adjuvant chemotherapy + radiotherapy.

- Adjuvant Hormone therapy is given based on receptor status positivity and usually after completion of chemotherapy.
- *Trastuzumab/Herceptin* can be given in Her2 positive tumours concurrently with chemotherapy.

LOCOREGIONAL RECURRENCE



ET – endocrine therapy

CT – chemotherapy

RT – radiotherapy

METASTATIC BREAST CANCER

- Palliative Simple mastectomy if ulcerated / fungated followed by Radiotherapy.
- Hormone therapy if ER+
- Bisphosphonates for bone metastasis.
- Herceptin → for Her2-neu positive tumours
- Chemotherapy →
    a. ER negative cancers,
    b. Symptomatic visceral metastasis,
    c. Hormone non responsive metastasis.
- Radiotherapy →
    - ✓ Painful bone metastasis
    - ✓ Brain metastasis
    - ✓ Painful or fungating soft tissue masses

MATERIALS
AND
METHODS

MATERIALS AND METHODS

This is a prospective and retrospective study done in patients with biopsy proven carcinoma breast who had undergone Mastectomy in Rajiv Gandhi Government General Hospital.

Inclusion criteria:

All women with carcinoma breast who had undergone mastectomy in Rajiv Gandhi Government General Hospital in the past 2 years and their resected specimen tested for receptor status by pathologists.

Exclusion criteria:

Those patients in whom the receptor status of mastectomy specimen was not studied or not available.

Sample size: 200 patients

Parameters studied: Estrogen receptor, Progesterone receptor, Her2/neu receptor by using special kits.

OBSERVATION
AND
ANALYSIS

OBSERVATION AND ANALYSIS

AGE DISTRIBUTION

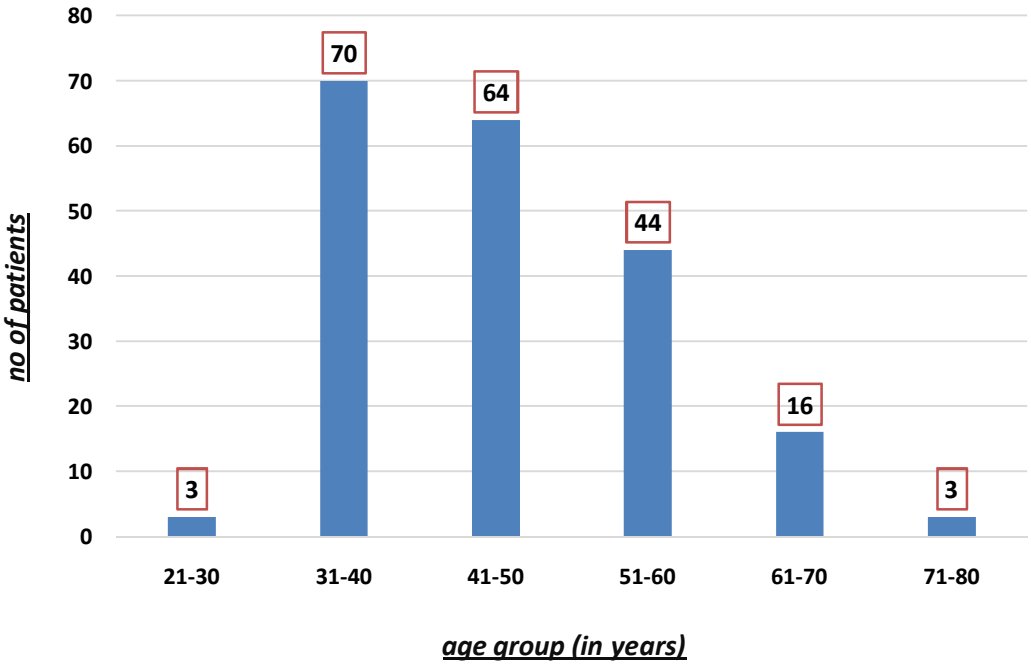
AGE GROUP (years)	NO. OF PATIENTS
21-30	3
31-40	70
41-50	64
51-60	44
61-70	16
71-80	3

BASED ON MENSTRUAL STATUS

Premenopausal – 120 patients

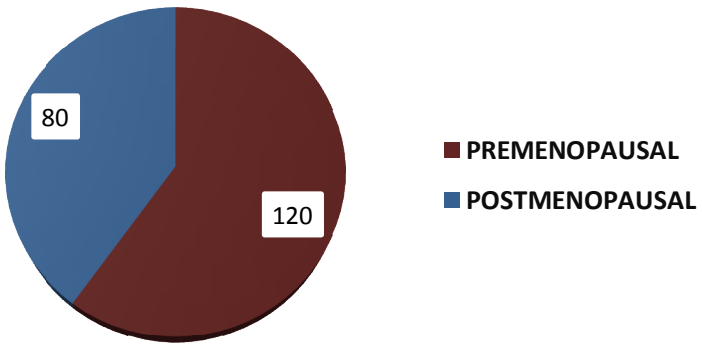
Postmenopausal – 80 patients

AGE DISTRIBUTION



Most of the patients belonged to the age groups 31-40 yrs (70 pts), 41-50 yrs (64pts) and 51-60 yrs (44 pts).

MENSTRUAL STATUS

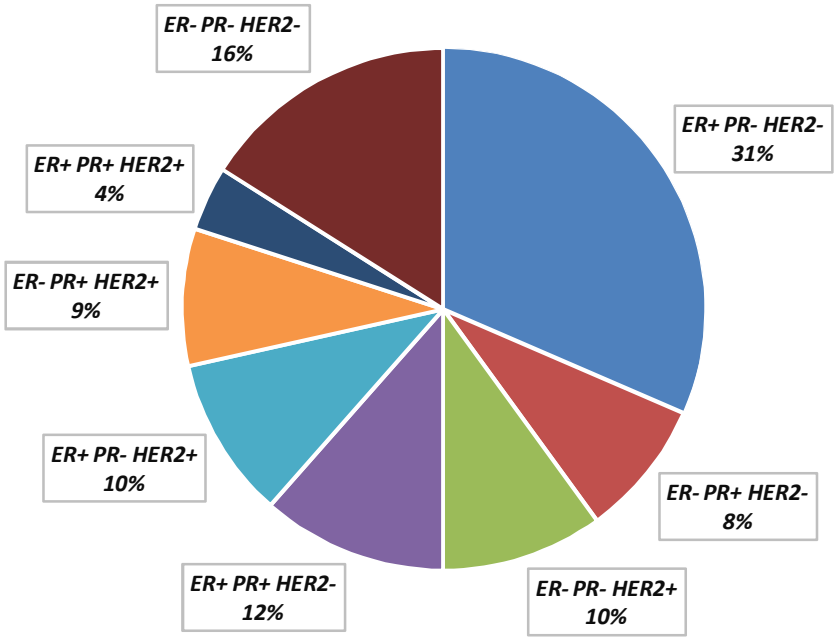


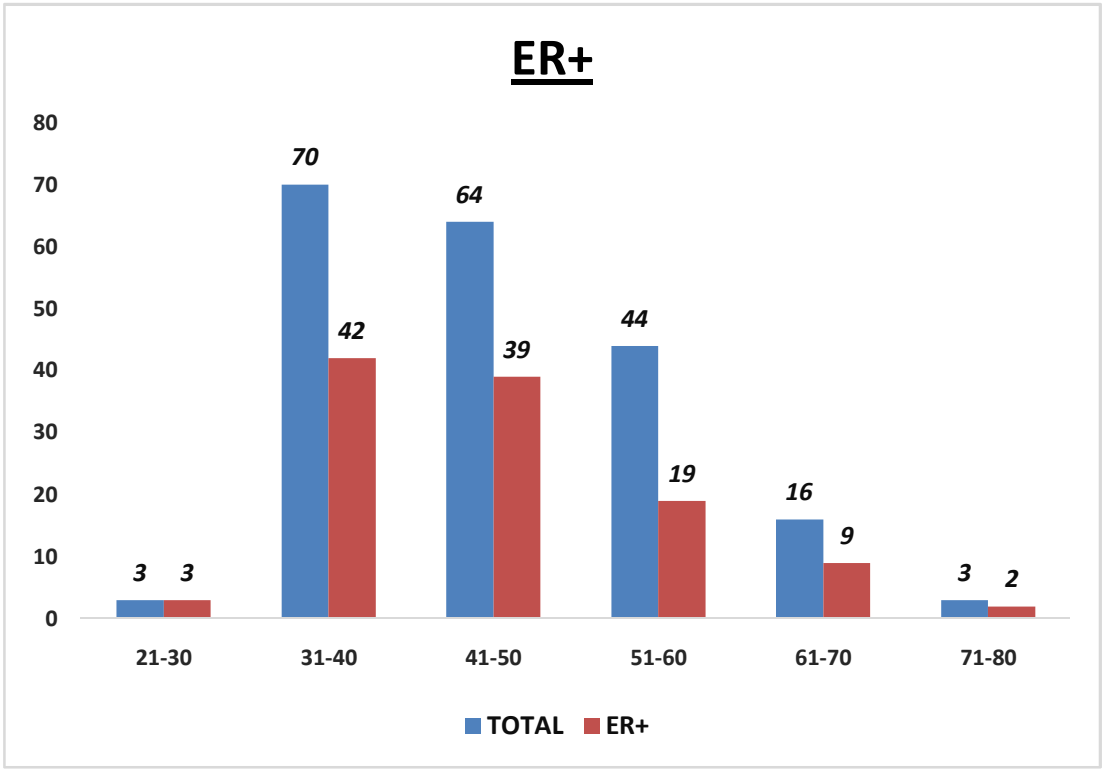
HORMONE RECEPTOR STATUS

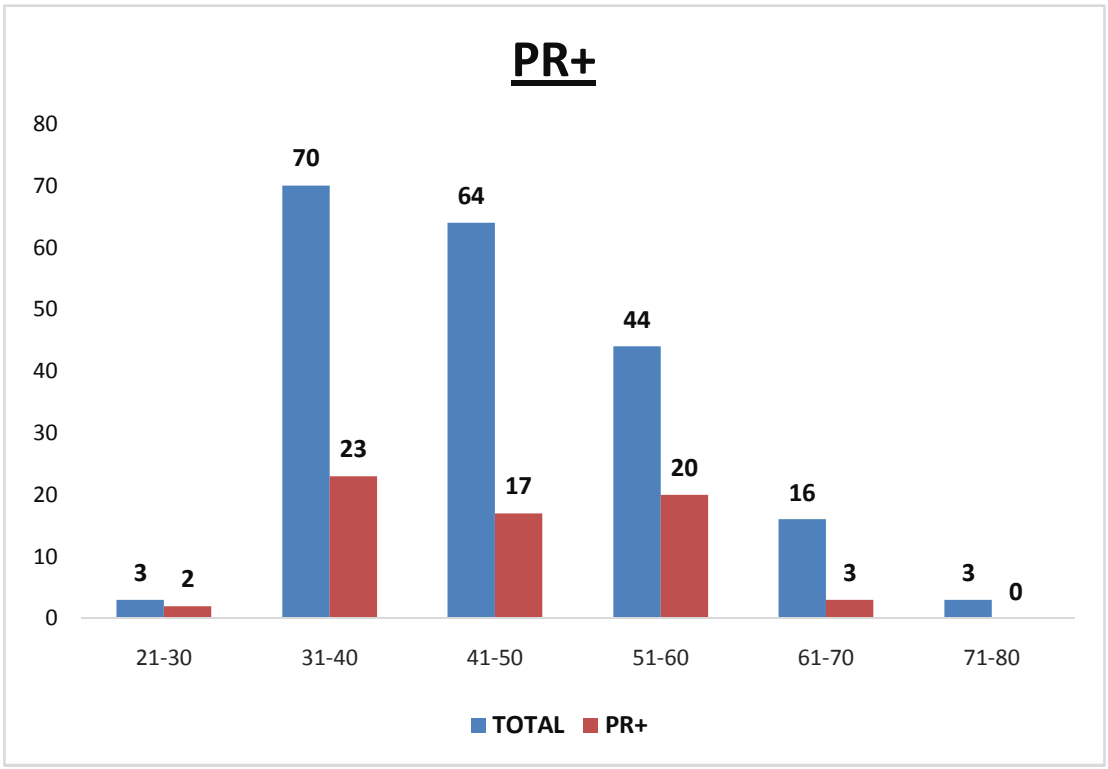
AGE GROUP (YRS)	**ER+ PR- HER2 -**	**ER- PR+ HER2 -**	**ER- PR- HER2 +**	**ER+ PR+ HER2 -**	**ER+ PR- HER2 +**	**ER- PR+ HER2 +**	**ER+ PR+ HER2 +**	**ER- PR- HER2 -**
21-30	**1**	**-**	**-**	**2**	**-**	**-**	**-**	**-**
31-40	**23**	**5**	**10**	**10**	**6**	**5**	**3**	**8**
41-50	**24**	**4**	**3**	**4**	**7**	**5**	**4**	**13**
51-60	**9**	**8**	**5**	**5**	**4**	**6**	**1**	**6**
61-70	**5**	**-**	**2**	**2**	**2**	**1**	**-**	**4**
71-80	**1**	**-**	**-**	**-**	**1**	**-**	**-**	**1**
TOTAL	**63**	**17**	**20**	**23**	**20**	**17**	**8**	**32**

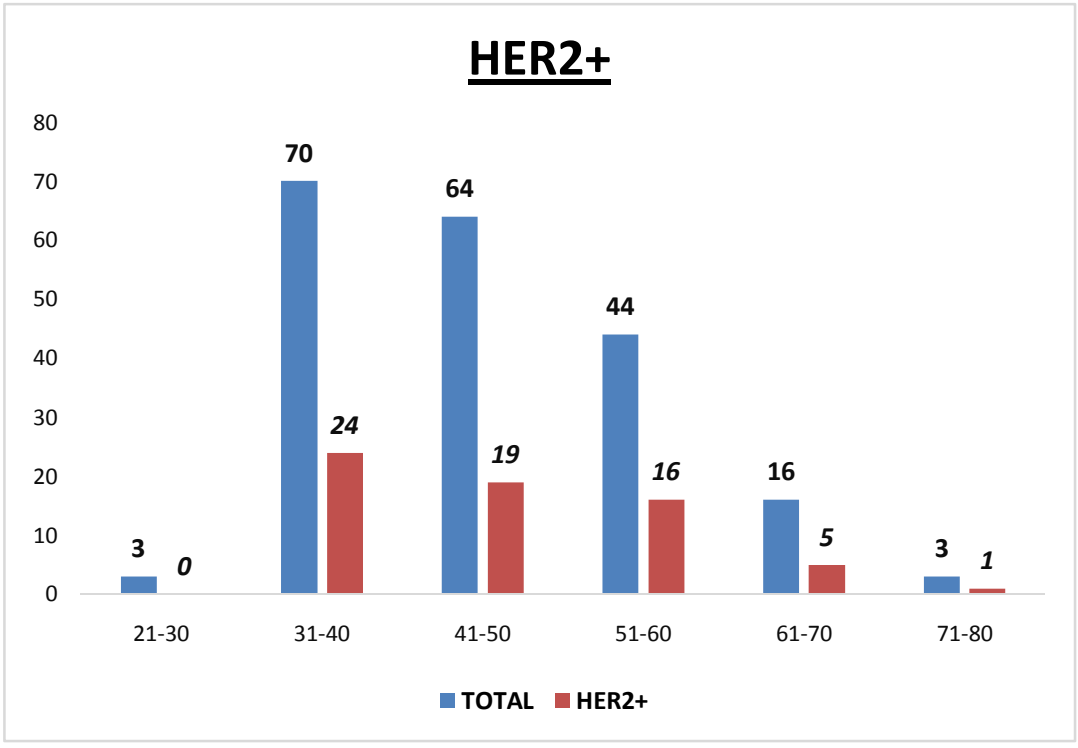
The most common type was found to be *ER+ PR- Her2-* and the least common was *Triple Positive* type.

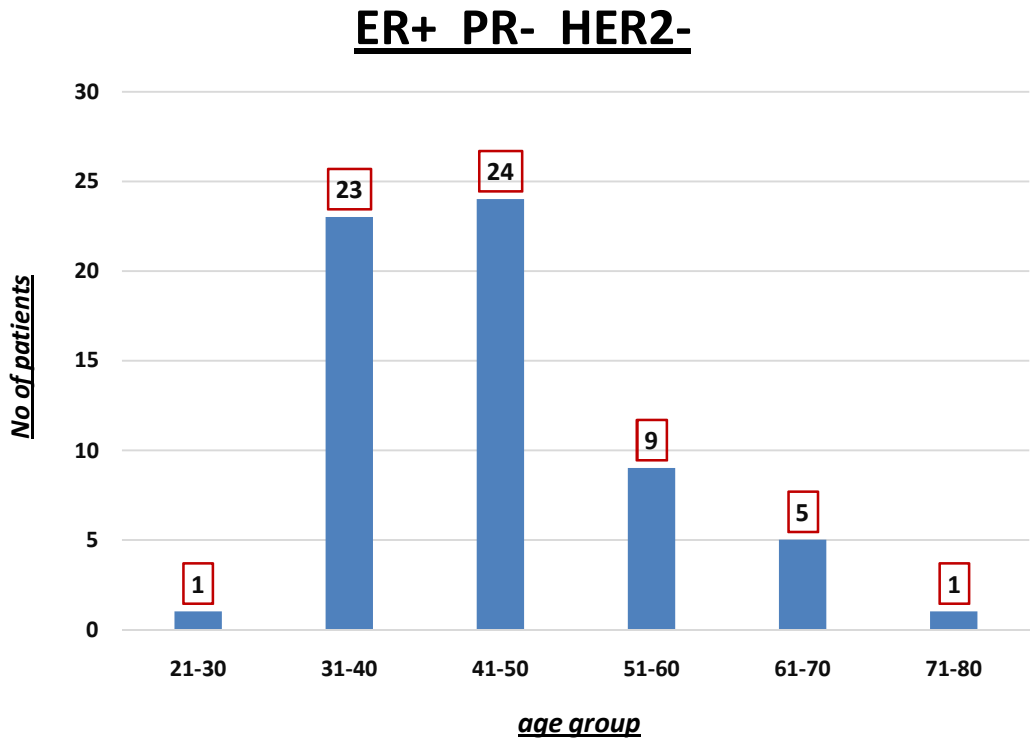
RECEPTOR STATUS



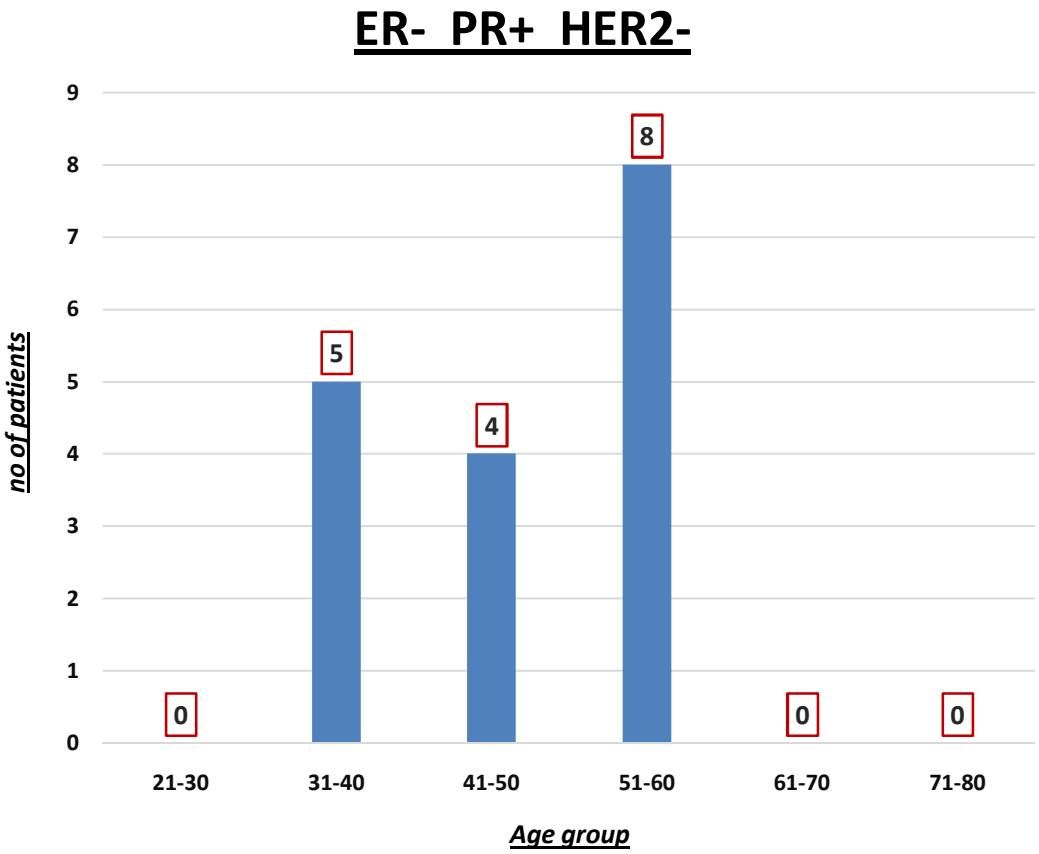



PR+
80
70
60
50
40
30
20
10
0
3
2
70
23
64
17
44
20
16
3
3
0
21-30
31-40
41-50
51-60
61-70
71-80
TOTAL
PR+

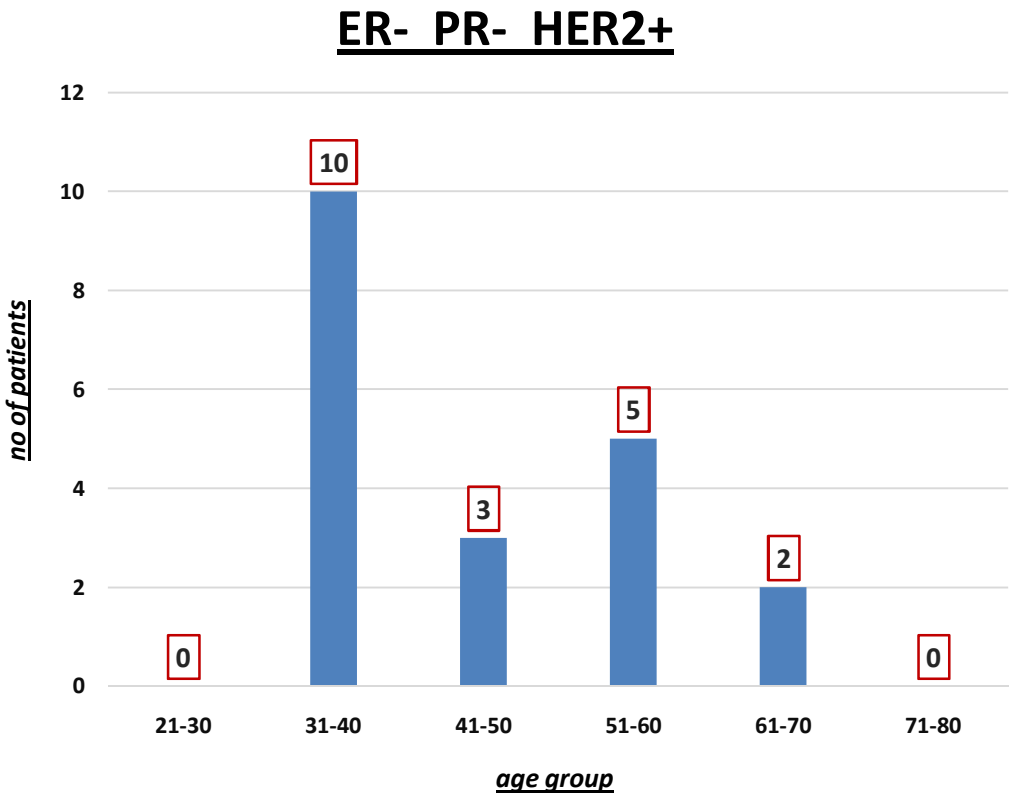

HER2+
80
70
60
50
40
30
20
10
0
3
0
70
24
64
19
44
16
16
5
3
1
21-30
31-40
41-50
51-60
61-70
71-80
TOTAL
HER2+



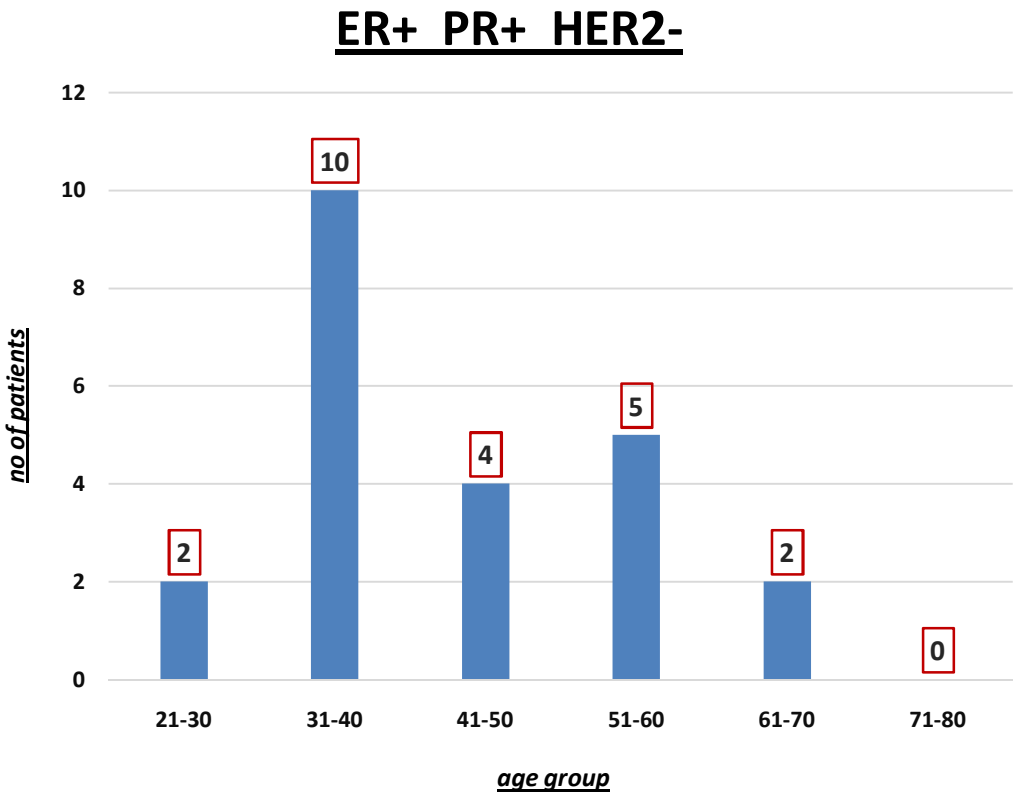
Estrogen Receptor alone was positive in 63 patients. It was common in age groups 41-50 yrs and 31-40 yrs.



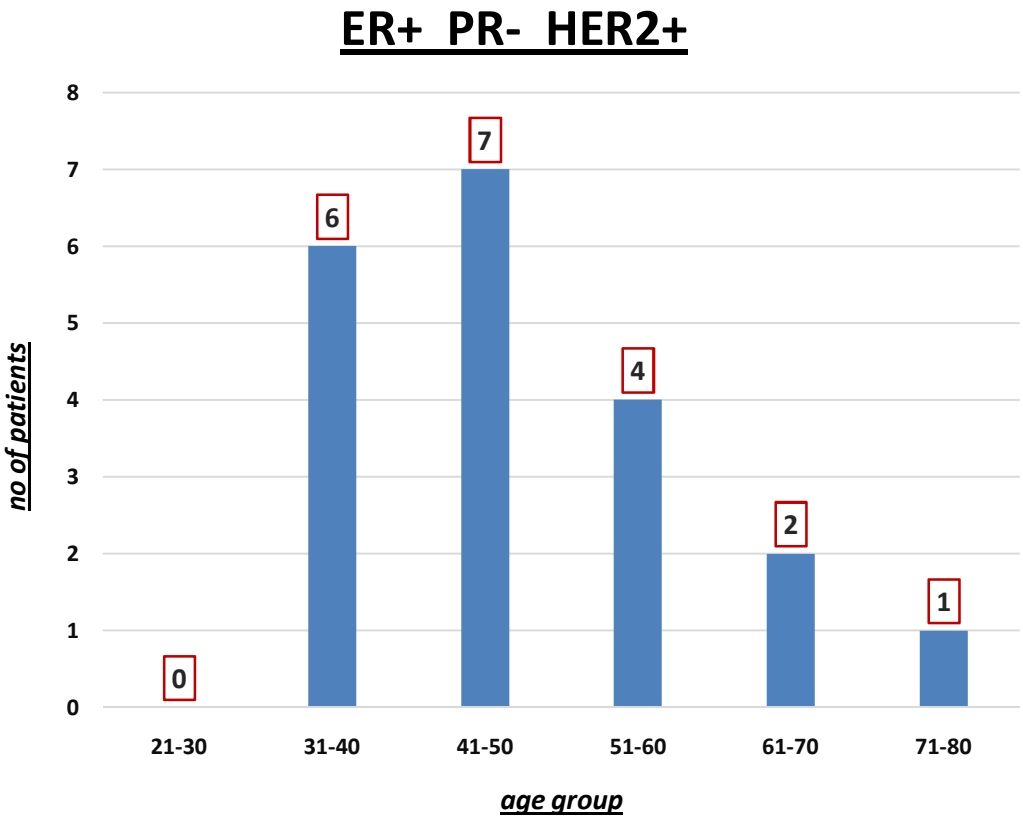
Progesterone Receptor alone was positive in 17 patients. It was seen in age groups 51-60 yrs, 31-40 yrs and 41-50 yrs.



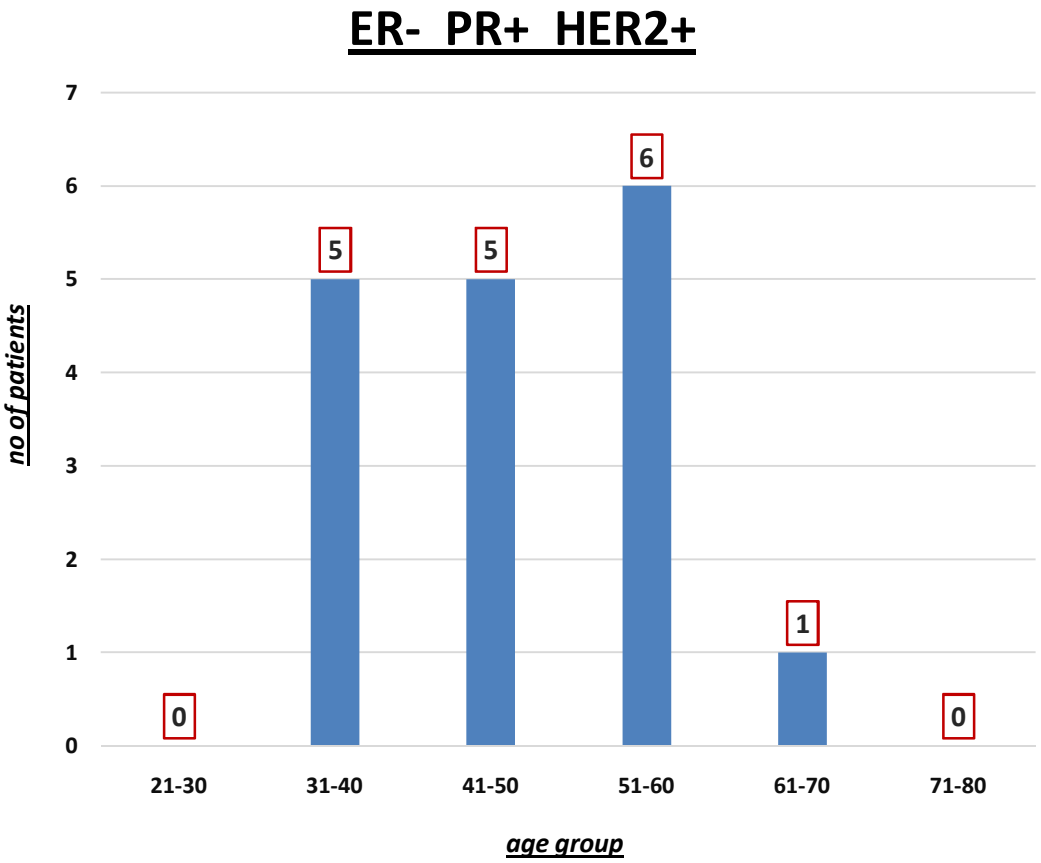
Her2 neu receptor alone was positive in 20 cases. It was most common in the age group 31-40 years (50% cases).



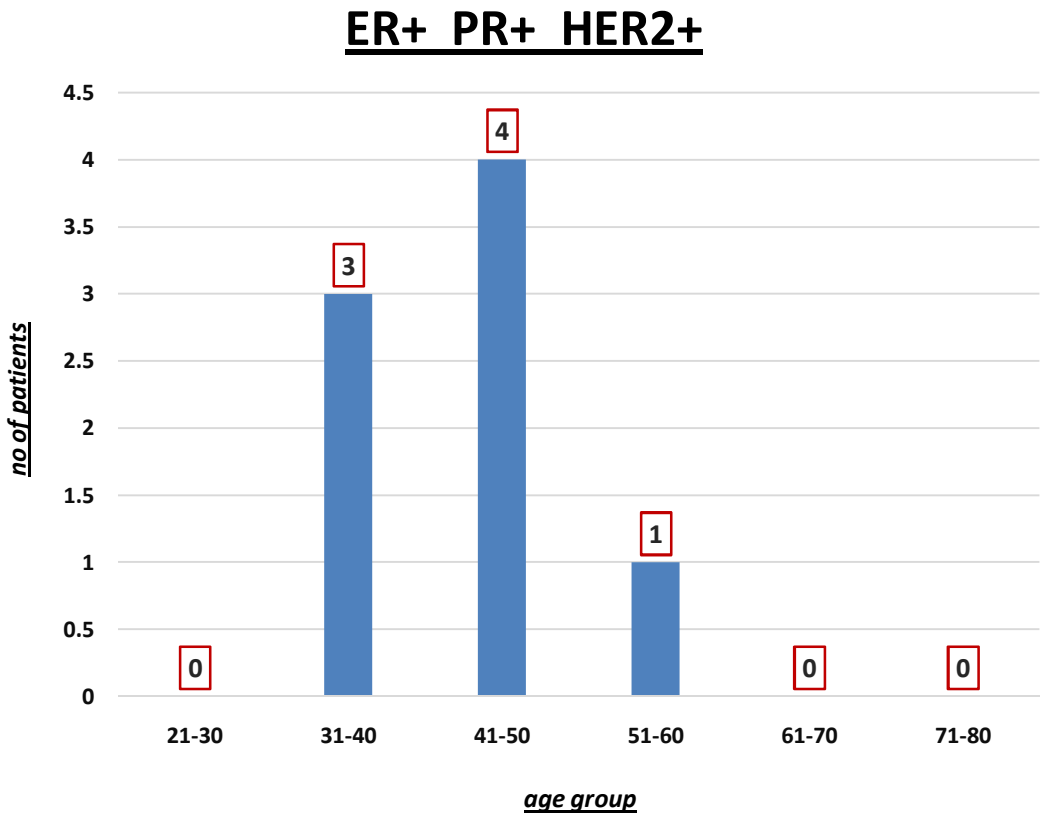
Both ER and PR were positive in 26 cases and the highest was in the age group 31-40 years (almost 40%).



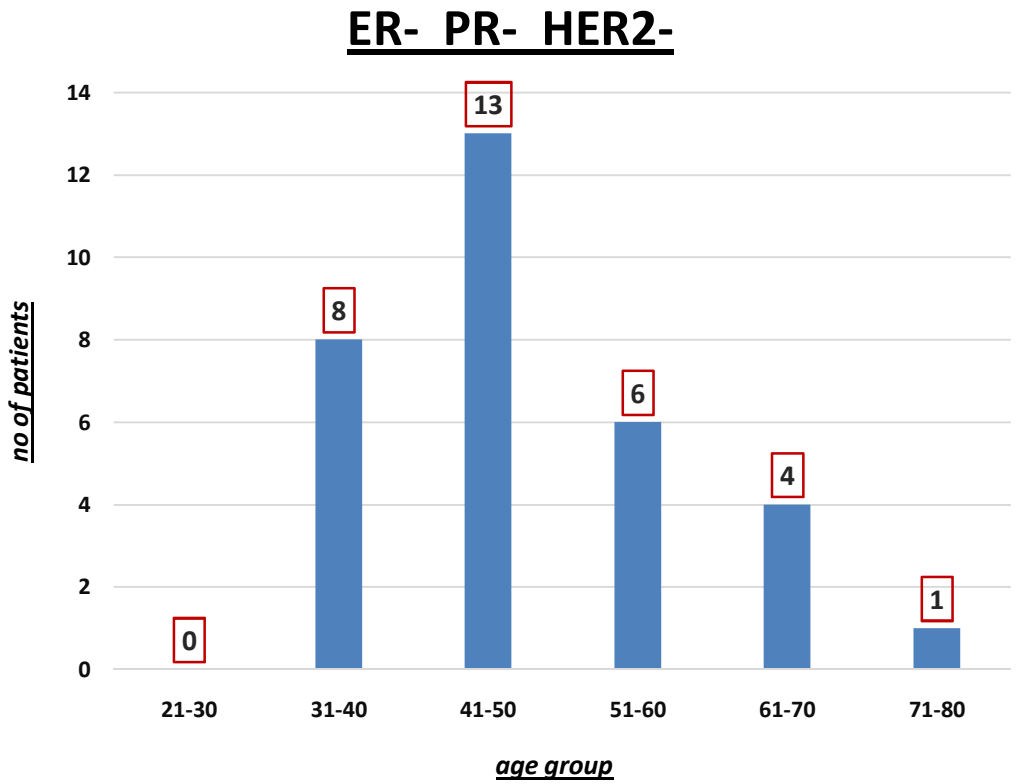
Both ER and Her2/neu receptor were positive in 20 patients. The highest was among the age groups 41-50 yrs (35%) & 31-40 yrs (30%).



Both PR and Her2 neu receptor were positive in 17 cases. The highest was among the age group 51-60 yrs (6 cases) followed by 41-50 and 31-40 yrs (5 cases each).



All the three receptors were found to be positive in 8 cases with the highest being in the age group 41-50 yrs (4 cases) followed by 31-40 yrs (3 cases) and 51-60 yrs (1 case).

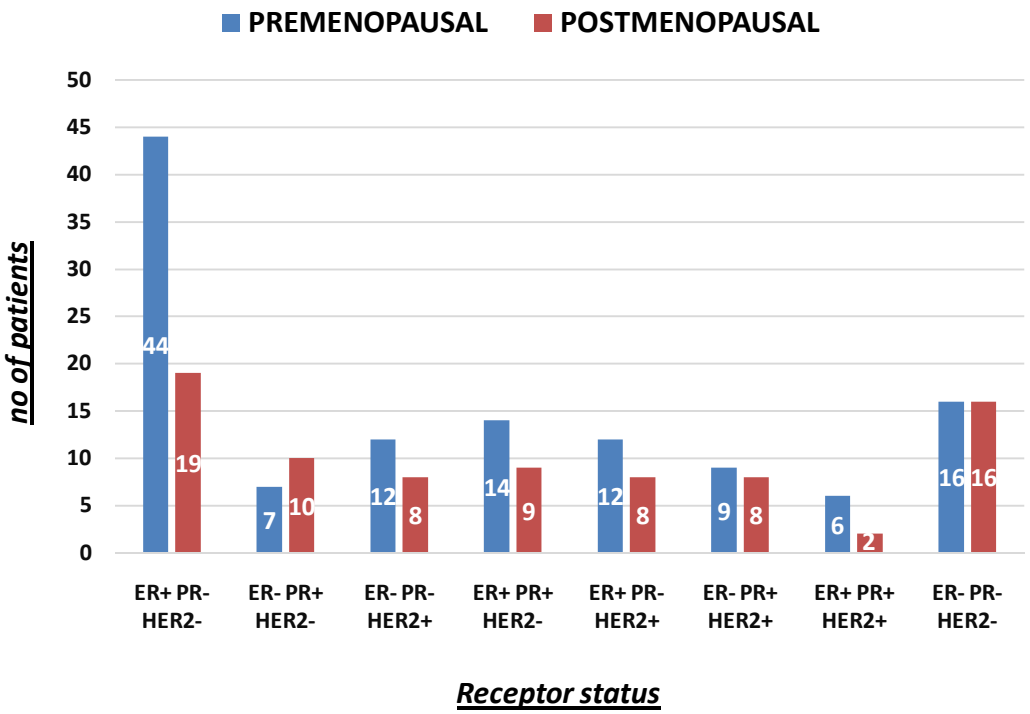


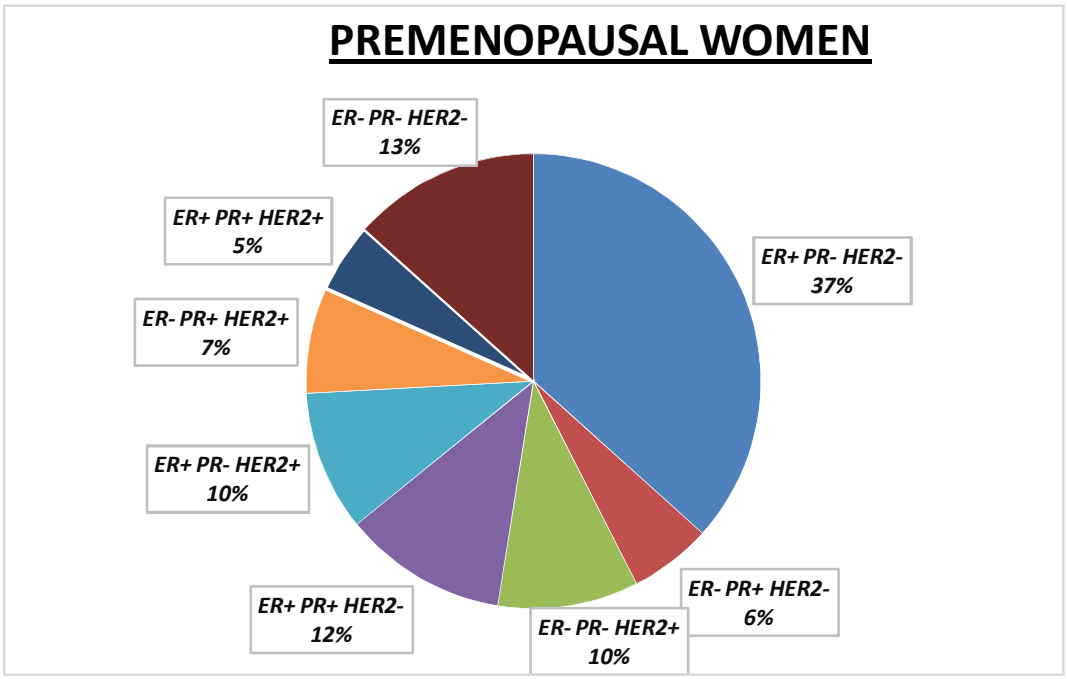
Triple negative cancers contributed to 32 cases (16%). The highest was in the age group 41-50 years (13) followed by 31-40 yrs (8) and 51-60 yrs (6).

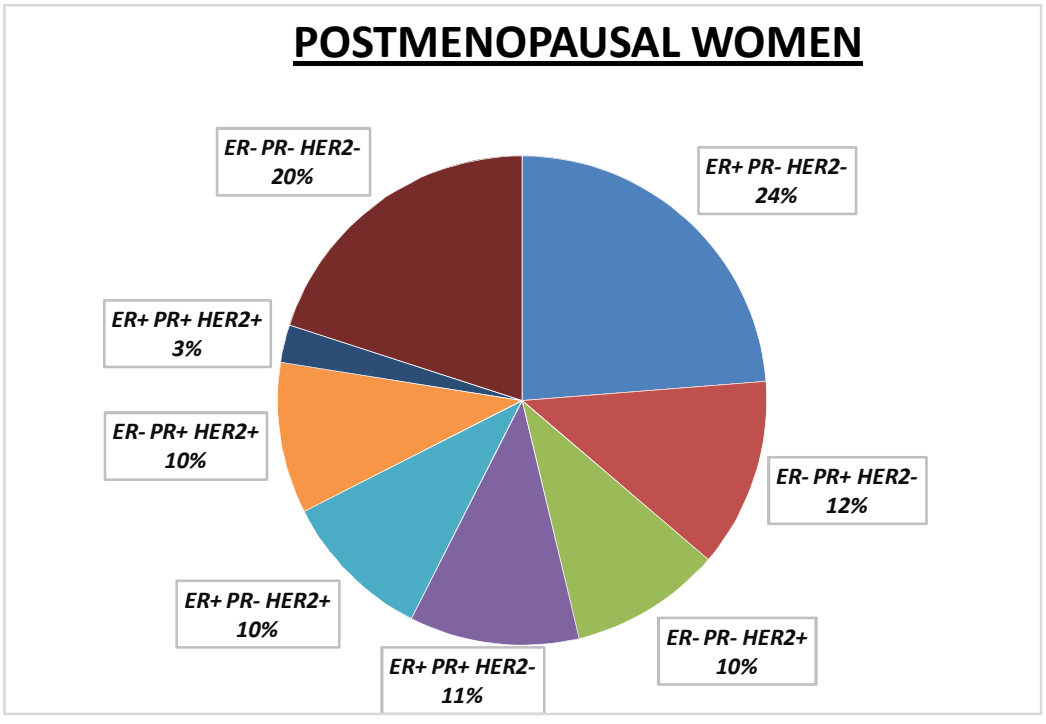
RECEPTOR DISTRIBUTION BASED ON MENSTRUAL STATUS

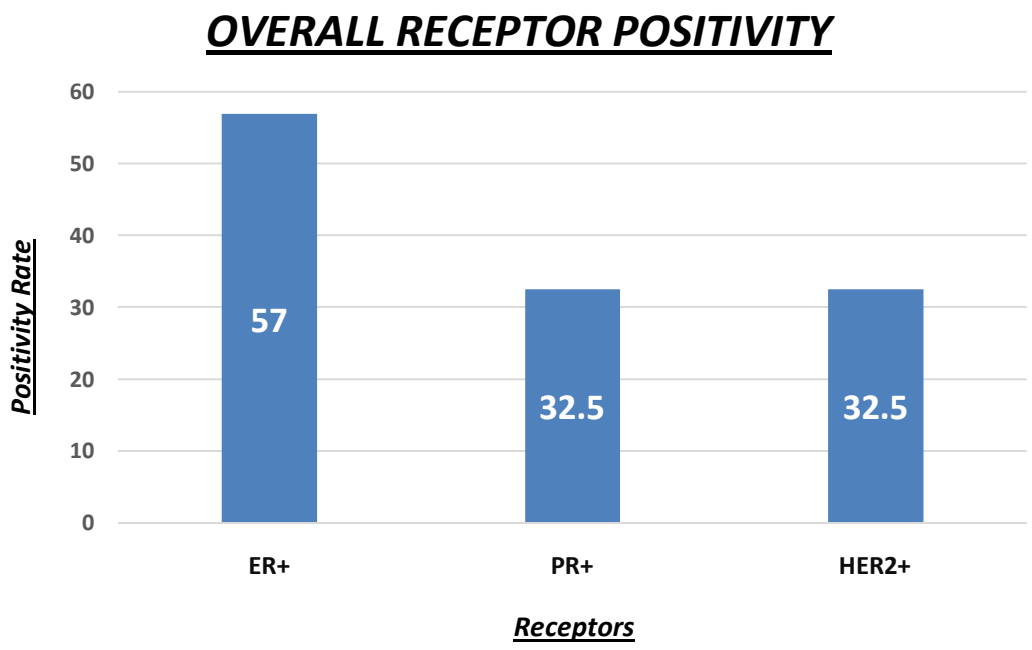
Menstrual status	ER+ PR- HER 2-	ER- PR+ HER 2-	ER- PR- HER 2+	ER+ PR+ HER 2-	ER+ PR- HER 2+	ER- PR+ HER 2+	ER+ PR+ HER 2+	ER- PR- HER 2-
Pre menopausal	44	7	12	14	12	9	6	16
Post menopausal	19	10	8	9	8	8	2	16
Total	63	17	20	23	20	17	8	32

RECEPTOR STATUS



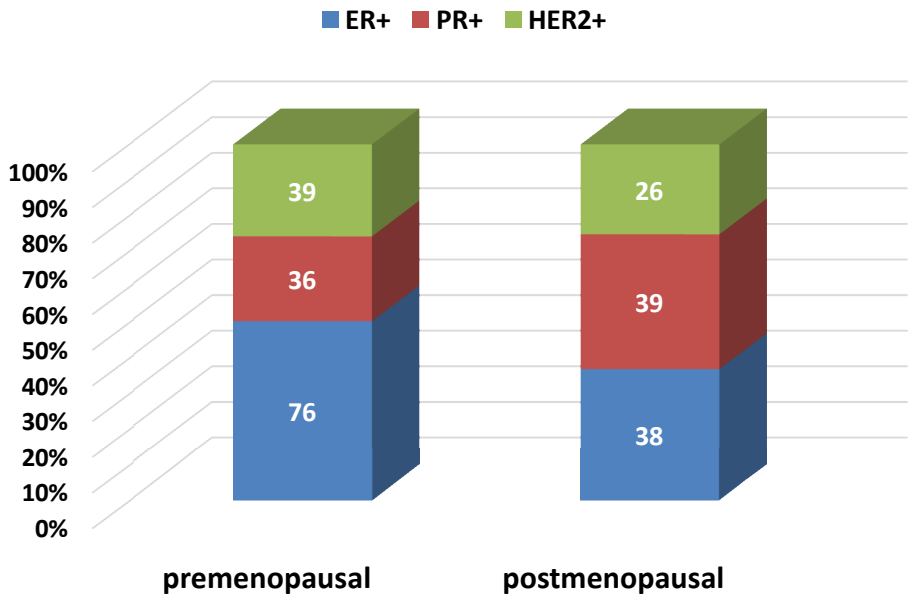

PREMENOPAUSAL WOMEN
ER- PR- HER2- 13%
ER+ PR+ HER2+ 5%
ER+ PR- HER2- 37%
ER- PR+ HER2+ 7%
ER+ PR- HER2+ 10%
ER+ PR+ HER2- 12%
ER- PR+ HER2- 6%
ER- PR- HER2+ 10%


POSTMENOPAUSAL WOMEN
ER- PR- HER2- 20%
ER+ PR- HER2- 24%
ER+ PR+ HER2+ 3%
ER- PR+ HER2+ 10%
ER- PR+ HER2- 12%
ER+ PR- HER2+ 10%
ER- PR- HER2+ 10%
ER+ PR+ HER2- 11%



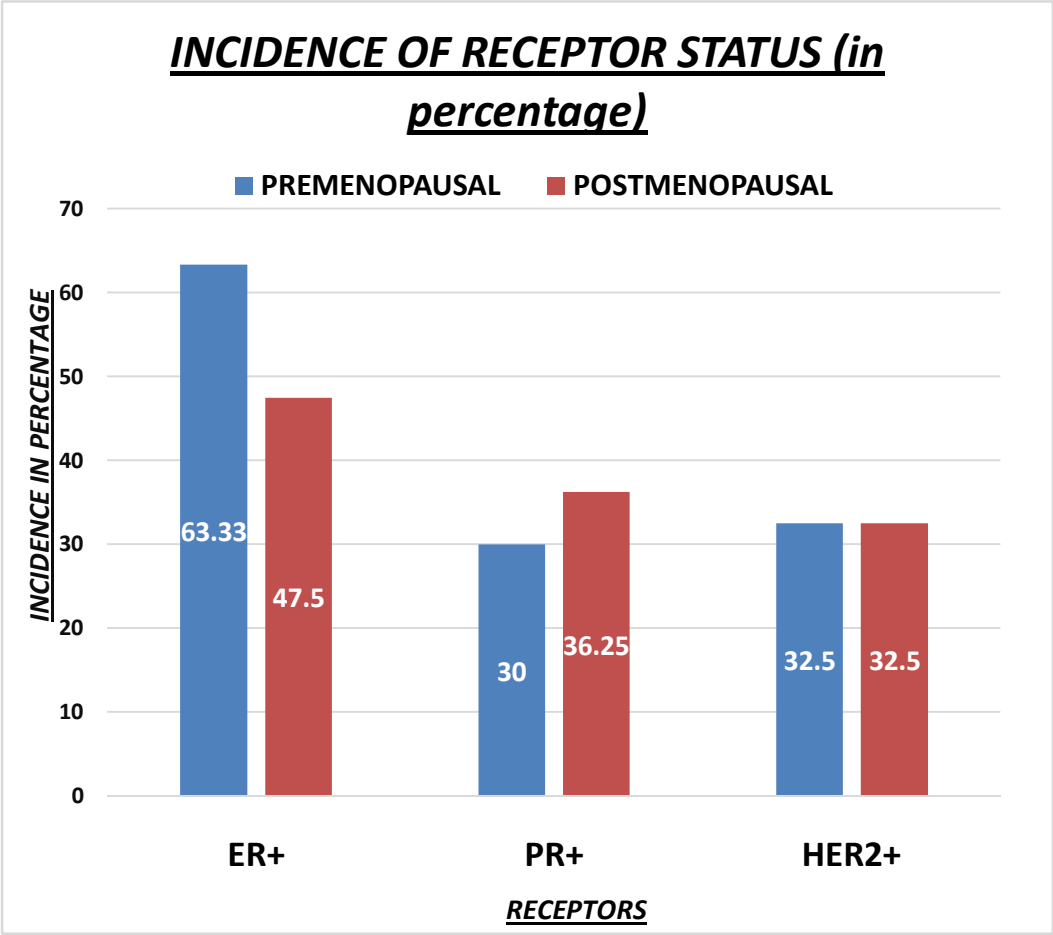
- Estrogen receptors were positive in 57% of the study population.
- Progesterone receptors were positive in 32.5% of the study population.
- Her2-neu receptors were positive in 32.5% of the study population.

DISTRIBUTION OF RECEPTORS



- The relative proportion of estrogen receptor positivity was high among premenopausal women whereas that of progesterone receptor was comparatively high among postmenopausal women.

- Her2 neu receptor was almost equally distributed among the two groups.



- The incidence of estrogen receptor is high in pre-menopausal age group whereas that of progesterone receptor status in postmenopausal women.

- Her2/neu receptor is equally distributed between the two groups.

DISCUSSION

DISCUSSION

The study aims at determining the incidence of receptor positive status in the mastectomy specimen of women operated for breast cancer in our hospital.

200 women who had been operated for breast cancer were selected for my study. Out of them, 120 (60%) were premenopausal women and 80 (40%) were postmenopausal women.

As per published literature, the incidence of receptor positivity varies in people of different races and ethnicity. The incidence of Estrogen and Progesterone receptor positivity increases with age and this is greater for progesterone than for estrogen receptors. Her2 positive and triple negative cancers tend to present at an earlier age.

In my study, the overall receptor positivity rate including both individual and combined status were 57% , 32.5% and 32.5% for ER, PR, HER2/neu receptors respectively.

Overall, the most common subtype was ER+ PR- HER2- contributing 31.5% of cases. The least common type was Triple positive accounting for 4% of cases. The same was true for either of the two groups as well.

ER+ tumours were more common in the younger age groups (100% in 21-30 yrs, 61% in 41-50 yrs, 60% in 31-40 yrs.) and also in 71-80 years (67%).

PR+ tumours were common in the age groups 21-30 yrs (67%), 51-60 yrs (45%), 31-40 yrs (33%) and 41-50 years (27%).

Her2/neu positive tumours were almost equally distributed in all age groups contributing around 30% in each (except in 21-30 age group in whom none were positive).

Triple negative tumours contributed for 16% of all cases.

ER positivity was proportionately more among premenopausal women (63.33% vs 47.5%), whereas PR positivity was proportionately more among postmenopausal women (36.25% vs 30%). Her2/neu receptors were equally distributed among both the groups (32.5%).

CONCLUSION

CONCLUSION

- The incidence of Estrogen receptor positivity was found to be 57%. It was higher in premenopausal women (63.33%), whereas in postmenopausal women it was 47.5%.

- The incidence of Progesterone receptor positivity was 32.5%. It was higher in postmenopausal women (36.25%) compared to premenopausal women (30%)

- The incidence of Her2/neu receptor positivity was found to be 32.5%. It was equally distributed in premenopausal and postmenopausal women (32.5%).

- The most common receptor subtype was *ER+ve, PR-ve, Her2/neu-ve* contributing 31.5%.

- The least common receptor subtype was *Triple positive* constituting 4%.

- The incidence of Triple negative receptor status was found to be 16%.

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ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு

மார்பக புற்றுநோய் உள்ள நோயாளிகளின் மார்பக திசுக்களை அறுவை சிகிச்க்குப்பின் திசு பரிசோதனை செய்து வாங்கி (ரிசப்டார்) i) ER, PR, HER-2/ Neu பரிசோதனை செய்யும் ஆராய்ச்சி

பெயர்	:	தேதி	:
வயது	:	உள் நோயாளி எண்	:
பால்	:	ஆராய்ச்சி சேர்க்கை எண்	:

இந்த ஆராய்ச்சின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் பங்கு பெறுகின்றேன். இந்த ஆராய்ச்சியில் இருந்து நான் எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

நான் இந்த ஆராய்ச்சியின் விபரங்களைக் கொண்ட ஆராய்ச்சித் தகவல் தாளைப் பெற்றுக் கொண்டேன்.

இதன் மூலம் எந்த பின்விளைவும் ஏற்படாது என்று மருத்துவர் மூலம் தெரிந்து கொண்டு, நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதம் தெரிவிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நாள் :
இடம் :

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜீவ்காந்தி அரசு பொது மருத்துவமனைக்கு வரும் நோயாளிகளில் மார்பக புற்றுநோய் உள்ள நோயாளிகளின் மார்பக திசுக்களை அறுவை சிகிச்க்குப்பின் திசு பரிசோதனை செய்து வாங்கி (ரிசப்டார்) i) ER, PR, HER-2/ Neu பரிசோதனை செய்யும் ஆராய்ச்சி இங்கு நடைபெறுகிறது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் உங்களுக்கு பரிசோதனைகள் செய்து அதன் தகவல்களை ஆராய்வோம். அதனால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துக்கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்பு சிகிச்சையின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள் :
இடம் :

PROFORMA

PROFORMA

Name: **Age:** **Sex:**

IP No.:

DOA: **DOP:** **DOD:**

Diagnosis:

Procedure Done:

On examination:

General condition:

VITALS:

PR: BP: RR:

CVS:

RS:

P/A:

SPECIMEN:

HISTO-PATHOLOGICAL EXAMINATION:

RECEPTOR STATUS:

Investigation parameters:

ER	
PR	
HER-2/neu	

Post-Operative Complications:
Wound infection:
Seroma formation:
Flap necrosis:

Condition on discharge:

MASTER CHART

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Latha	34	23415	Premenopausal	+	+	-
Gowri	50	46712	Post-menopausal	+	-	-
Fathima	43	124561	Premenopausal	+	-	-
Sindhu	28	87645	Premenopausal	+	-	-
Meena	45	67564	Premenopausal	-	+	-
Mariyammal	38	54627	Premenopausal	+	-	-
Ettiyammal	40	145631	Premenopausal	+	+	-
Padma	36	87634	Premenopausal	+	-	-
Radha	39	56742	Premenopausal	+	-	+
Gomathi	34	98765	Premenopausal	+	+	-
Selvi	45	14568	Premenopausal	+	-	-
Kuppammal	56	35427	Post-menopausal	-	-	-
Manjula	35	74883	Premenopausal	-	+	+
Parvathiammal	48	78771	Post-menopausal	+	-	-
Yamuna Devi	40	46789	Premenopausal	+	+	-
Lakshmi	32	35672	Premenopausal	+	-	-
Usha Devi	46	98788	Premenopausal	+	-	-
Saroja	60	21876	Post-menopausal	-	+	-
Dhanalakshmi	43	80093	Premenopausal	-	-	+
Kavitha	38	68090	Premenopausal	+	-	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Pushpa	45	78564	Premenopausal	+	-	-
Logeshwari	41	67584	Premenopausal	-	-	+
Jayalakshmi	56	35647	Post-menopausal	+	-	-
Jayashree	37	99876	Premenopausal	+	+	-
Janaki	68	56709	Premenopausal	-	-	+
Poornima	50	13456	Post-menopausal	+	-	-
Pavithra	45	84561	Premenopausal	+	-	-
Bhuvana	35	98789	Premenopausal	-	+	+
Devaki	59	76584	Post-menopausal	+	-	-
Fathima	46	74562	Premenopausal	+	-	-
Gajalakshmi	39	46701	Premenopausal	+	+	-
Indira	30	57890	Premenopausal	+	+	-
Saradha	45	36578	Premenopausal	+	-	+
Saritha	52	25364	Post-menopausal	+	+	-
Sandhya	43	44567	Premenopausal	+	-	-
Meenatchi	63	22447	Post-menopausal	-	-	-
Lalitha	40	44352	Premenopausal	+	+	-
Kumari	57	66745	Post-menopausal	-	+	+
Komaladevi	47	54637	Premenopausal	+	-	-
Radha	52	134256	Post-menopausal	+	+	+

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Logeshwari	35	34568	Premenopausal	-	-	-
Namitha	38	28765	Premenopausal	-	-	+
Vimala	40	98734	Premenopausal	-	-	+
Suguna	47	56078	Premenopausal	+	-	-
Sumathi	38	56987	Premenopausal	-	+	-
Thangammal	60	12986	Post-menopausal	+	-	-
Dhanammal	55	69435	Post-menopausal	+	+	-
Eswari	71	128945	Post-menopausal	+	-	-
Lakshmi	57	56984	Post-menopausal	-	-	+
Rajeshwari	40	47265	Premenopausal	-	-	+
Divya	32	20895	Premenopausal	+	-	-
Bharathi	37	86942	Premenopausal	-	-	+
Rani	47	12659	Post-menopausal	+	+	-
Ambika	44	45692	Premenopausal	+	-	-
Roopika	38	20365	Premenopausal	+	+	+
Geetha	45	87803	Premenopausal	-	-	-
Nirmala	51	30658	Post-menopausal	+	-	-
Nithya	38	45690	Premenopausal	+	-	-
Manjula	33	55694	Premenopausal	-	+	+
Maragadham	56	22605	Post-menopausal	-	+	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Kala	41	45673	Premenopausal	-	-	-
Nazeema begum	46	23687	Premenopausal	+	-	-
Krishnaveni	33	85541	Premenopausal	+	-	-
Pappammal	48	65983	Premenopausal	+	-	-
Kavitha	39	125698	Premenopausal	-	-	+
Dhanalakshmi	50	14589	Post-menopausal	-	+	+
Sindhu	44	56421	Premenopausal	-	-	-
Gomathi	49	20215	Premenopausal	+	-	+
Latha	55	30502	Post-menopausal	+	-	+
Kamala	62	89504	Post-menopausal	+	-	+
Janaki	72	45069	Post-menopausal	+	+	-
Logammal	42	58320	Premenopausal	+	-	-
Neelamma	39	96172	Premenopausal	+	+	-
Padma	34	18640	Premenopausal	-	+	+
Parvathy	44	29052	Post-menopausal	-	-	-
Saritha	51	50680	Post-menopausal	-	-	-
Ananya das	31	49158	Premenopausal	-	+	-
Mary	33	26598	Premenopausal	+	-	+
Reena	40	65654	Premenopausal	+	+	-
Kartika	36	85985	Premenopausal	-	-	+
Muniyammal	46	44485	Premenopausal	+	-	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Poongodhai	55	34570	Post-menopausal	-	-	-
kumari	43	25613	Premenopausal	+	-	-
Jayanthi	50	21445	Post-menopausal	-	-	-
Malar	47	65986	Post-menopausal	+	+	+
Madhumitha	33	86059	Premenopausal	-	-	+
Radhika	40	56902	Premenopausal	+	-	+
Saranya Devi	31	45750	Premenopausal	-	-	+
Gayathri	38	55690	Premenopausal	+	+	+
Ambika	58	58740	Post-menopausal	+	-	+
Neela	45	26542	Post-menopausal	+	-	-
Andalammal	61	86980	Post-menopausal	+	-	-
Kondamma	39	78930	Premenopausal	-	-	-
Fathima	53	23547	Post-menopausal	+	-	-
Bhuvana	49	76026	Premenopausal	+	-	-
Preethi	33	80594	Premenopausal	+	-	+
Divya bharathi	41	36504	Premenopausal	-	-	-
Ellammal	48	56029	Post-menopausal	-	+	-
Akila	40	48500	Premenopausal	+	+	+
Pushpalatha	51	56980	Post-menopausal	-	+	-
Pavithra	32	14582	Premenopausal	+	-	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Padma	45	56942	Premenopausal	+	-	+
Ramya	31	73650	Premenopausal	+	-	-
Sivayogana	30	63201	Premenopausal	+	+	-
Julie	44	118710	Premenopausal	-	-	-
Deepika	34	65487	Premenopausal	-	-	-
Nithya	40	45692	Premenopausal	+	-	-
Thulasi	61	102598	Post-menopausal	-	+	+
Deepa	40	36548	Premenopausal	+	-	-
Kartika	34	45897	Premenopausal	+	-	+
Anjali	45	25647	Premenopausal	+	-	-
Radha	62	48621	Post-menopausal	-	-	-
Mounammal	50	80015	Post-menopausal	+	-	-
Thulasidurga	33	75946	Premenopausal	-	-	+
Devi	33	15973	Premenopausal	+	-	-
Nagamani	51	26842	Post-menopausal	+	-	-
Pitchaiammal	64	95864	Post-menopausal	+	-	-
Sengammal	52	125984	Post-menopausal	-	+	-
Visalakshi	65	56982	Post-menopausal	-	-	+
Raniyammal	54	83548	Post-menopausal	-	-	+
Yogeshwari	42	24409	Premenopausal	+	-	+

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Angamma	52	45986	Post-menopausal	-	-	+
Sasirekha	37	23105	Premenopausal	-	-	-
Suganya	40	102519	Premenopausal	-	+	-
Anju	38	56942	Premenopausal	+	-	-
Nirmala	42	76952	Premenopausal	-	+	+
Vijaya	53	86245	Post-menopausal	+	-	-
Varalakshmi	39	98624	Premenopausal	+	-	-
Kumari	47	75601	Post-menopausal	-	-	-
Kanchana	55	30125	Post-menopausal	+	-	+
Bhuvaneshwari	51	120654	Post-menopausal	-	+	+
Shankari	47	56025	Post-menopausal	-	-	-
Kavitha	33	65986	Premenopausal	-	-	-
Anusha	36	99654	Premenopausal	+	-	-
Aswini	42	46249	Premenopausal	-	+	+
Sarala	62	68521	Post-menopausal	-	-	+
Saradha	60	121450	Post-menopausal	-	+	+
Banu	44	88659	Premenopausal	-	+	+
Meenalotchini	57	56981	Post-menopausal	+	-	-
Yamuna	56	66224	Post-menopausal	-	+	+
Jamuna Devi	62	18642	Post-menopausal	+	-	+

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Durga	52	56901	Post-menopausal	-	+	-
Baby	56	126584	Post-menopausal	-	-	+
Sridevi	46	66942	Premenopausal	-	+	+
Pushpammal	48	33651	Post-menopausal	-	+	-
Gowri	61	42103	Post-menopausal	+	-	-
Anjalai	39	36987	Premenopausal	+	-	-
Geetha	56	10365	Post-menopausal	-	-	-
Jothi	37	100654	Premenopausal	+	-	-
Janani	41	98475	Premenopausal	+	-	-
Sushma	32	26597	Premenopausal	-	-	-
Nitya	40	46548	Premenopausal	+	-	-
Lavanya	42	99654	Premenopausal	+	+	+
Saradha	48	29731	Post-menopausal	-	-	-
Jothi	53	122378	Post-menopausal	-	-	-
Poovammal	58	16548	Post-menopausal	+	-	+
Nandhini	42	94584	Premenopausal	+	+	-
Malar	51	85785	Post-menopausal	-	-	-
Govindammal	60	75753	Post-menopausal	+	+	-
Farzana	47	62498	Premenopausal	+	+	-
Mallika	65	78536	Post-menopausal	-	-	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Govindammal	56	81627	Post-menopausal	+	-	-
Parameshwari	46	113932	Premenopausal	+	-	-
Andal	62	103165	Post-menopausal	+	-	-
Jayanthi	35	78962	Premenopausal	-	+	-
Vijaya	52	78911	Post-menopausal	-	+	+
Revathi	48	86728	Post-menopausal	-	-	+
Thilagavathy	39	34527	Premenopausal	+	+	-
Thangam	62	19587	Post-menopausal	+	+	-
Vaishnavi	50	65738	Post-menopausal	+	+	-
Yasodha	61	126573	Post-menopausal	+	-	-
Kiruthika	31	124560	Premenopausal	+	-	-
Logeshwari	37	96420	Premenopausal	-	-	+
Pushpa	41	22668	Premenopausal	+	-	-
Kasammal	55	45858	Post-menopausal	-	+	-
Poovammal	46	83940	Post-menopausal	+	-	+
Jothi	37	46698	Premenopausal	+	-	-
Aisha bee	75	55694	Post-menopausal	-	-	-
Poongodi	43	78595	Premenopausal	-	+	-
Kavya	38	64450	Premenopausal	-	-	-
Jothi	37	46698	Premenopausal	+	-	-

NAME	AGE	I.P.NO	STATUS	ER	PR	HER2
Rekha	46	56489	Premenopausal	+	-	-
Ranjana	35	44522	Premenopausal	-	-	-
Jainab kali	52	125586	Post-menopausal	-	+	-
Kala	57	69347	Post-menopausal	+	+	-
Ayesha	45	36940	Premenopausal	-	-	-
Kondammal	39	36520	Premenopausal	-	+	+
Yuvarani	36	69980	Premenopausal	+	-	-
Poornima	42	56694	Premenopausal	-	-	-
Harini	37	57420	Premenopausal	+	-	-
Elakiya	39	76487	Premenopausal	+	-	+
Rani	51	36521	Post-menopausal	-	+	-
Aishwarya	38	98732	Premenopausal	-	+	-
Yasodhammal	55	65421	Post-menopausal	-	-	+
Rojammal	43	66502	Premenopausal	+	+	+
Padmavathy	61	96520	Post-menopausal	-	-	-
Dhatchayini	42	102355	Premenopausal	+	+	+
Girija	44	54982	Premenopausal	+	-	+
Gunasundari	54	86420	Post-menopausal	+	+	-
Ambika	57	70264	Post-menopausal	-	+	+
Rani	47	89456	Premenopausal	+	-	+
Dhatchayini	42	102355	Premenopausal	+	+	+